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## ACADEMICIAN NIKOLAI SEMENOVICH KURNAKOV

(ON THE CENTENARY OF HIS BIRTH)

M. A. Klochko

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The centenary of the birth of Nikolai Semenovitch Kumakov, one of the most outstanding Russian chemists, will be celebrated in the current year (1960).

Through his studies on salts, alloys, ores, and organic materials, N. S. Kumakov not only enriched various branches of theoretical and applied chemistry but developed certain general principles which served as a basis for physical chemical analysis, a new field of chemistry dealing with the investigation of chemical systems.

Nikolai Semenovitch Kurnakov was born on December 6, 1860 in the city of Nalinsk in the former Vyatska district (now the Kirovskii province) in the family of an officer who had participated in the defence of Sevastopol in 1854-1855. After completing his studies in the Petersburg Institute of Mines in 1882, N. S. Kumakov continued on to serve there, first as a lecturer and then as professor of inorganic and analytical chemistry. He also served as professor of physical chemistry in the Electrotechnical Institute (1899-1908) and as professor of general chemistry in the Petersburg (now Leningrad) Polytechnic Institute (1902-1930).

N. S. Kumakov was elected to membership in the Academy of Sciences in 1913 and here organized (together with V. I. Vernadskii and A. E. Fersman) in 1915 a commission for studying the natural resources of Russia.

After the Great October Socialist Revolution, N. S. Kurnakov organized the Institute for Physical Chemical Analysis for the study of the properties of alloys, salt solutions, and organic substances. Mixtures of substances which are capable of interacting chemically with one another are designated as chemical systems. Kumakov proposed the name of physical chemical analysis for the branch of theoretical chemistry which deals with systems.

N. S. Kurnakov served as director not only of the Institute of Physical Chemical Analysis, but of the Academy of Sciences' Laboratory of General Chemistry, the successor to the chemical Laboratory founded by M. V. Lomonosov in 1748, as well as the Institute for the Study of Platinum and Other Noble Metals. In 1934, these three institutions were combined into a single Institute of General and Inorganic Chemistry of the Academy of Sciences of the USSR, which N. S. Kumakov directed until his death on March 19, 1941. This Institute was named in his honor in 1944.

N. S. Kumakov organized a number of scientific meetings, conferences, and congresses, such as the Mendeleev Congresses, and conferences on physical chemical analysis.

His work was recognized by the award of a Stalin Prize, the title of Honored Scientist of the RSFSR, and the order of the Red Banner of Labor.

N. S. Kurnakov worked in a number of fields of theoretical and applied chemistry, studying complex compounds, alloys, natural salts, and systems of organic substances. In these investigations he adhered to the principle of utilizing objectives of practical importance as a basis for theoretical studies.

The first extensive work of N. S. Kumakov was his dissertation on "The Complex Metallic Bases" which appeared in 1893. Here he laid down the basis for a systematic study of the complex compounds, which was



later continued in Russia by L. A. Chugaev and I. I. Chernyaev and their students and co-workers. In synthesizing complex platinum compounds and studying their properties, N. S. Kurnakov discovered the reaction which now carries his name. This reaction makes it possible to determine the geometrical structures of the compounds of divalent platinum from their reactions with thiourea, distinction being made between the trans compounds, in which identical groups are situated on opposite sides of the platinum atom, from the cis compounds, in which these groups are located on the same side of the platinum.

N. S. Kurnakov began his studies of metallic systems at the end of the last century. He considered that correct conclusions as to the nature of alloys could be obtained only after study had been made of a number of their physical chemical properties.

The study of alloys which N. S. Kurnakov carried out in conjunction with S. F. Zhemchuzhnyi, his partner in many years of work, disclosed a number of rules (subsequently designated as the Kurnakov-Zhemchuzhnyi Rules) relating the compositions and properties of binary metallic systems. Thus it was found that the conductivity isotherm (curve showing the variation of conductivity with concentration) for a system involving a solid solution would be a continuous curve with a minimum, while the hardness isotherm would pass through a maximum. The isotherms of these two properties approximate straight lines in the case of a two-phase mechanical mixture of crystals of the two metals. Special or singular points appear on these isotherms when the components form chemical compounds, and the compositions corresponding to them are those of the compounds themselves. N. S. Kurnakov proposed that such compounds be designated as "daltonides" (from the English scientist James Dalton) and distinguished from the berthollides, or compounds of variable composition whose existence had been predicted by the French scientist C. Berthollet. Berthollides had been found by N. S. Kurnakov in such metallic systems as thallium-bismuth and lead-sodium. The compositions of these compounds could be altered over wide intervals.

This study of solid solutions led to the discovery of alloys whose electrical resistance was high and weakly dependent on temperature. These substances are of much practical importance.

While studying the alloys of gold and copper, N. S. Kurnakov discovered an instance of the formation of a chemical compound from solid solutions. Other so-called Kurnakov compounds were later found in other metallic systems and are still studied intensively with a view to elucidating their nature and structure.

N. S. Kurnakov carried out an important work on the modernization of apparatus and techniques in the course of his studies on metallic systems. In 1903 he devised a registering pyrometer which permitted the automatic recording of the temperature during heating or cooling of a system. This Kurnakov pyrometer would be considered as a very refined instrument even at the present time, and it is still used not only for thermal analysis (the determination of the temperatures of melting, crystallization, phase transformations, etc.) but also for following any process which is accompanied by an alteration in the electromotive force. N. S. Kurnakov constructed special equipment for a study of flow pressures which he carried out in conjunction with S. F. Zhemchuzhnyi.

From the publication of his paper on "Volatile Saltworks Systems" in 1885 to the very last years of his life, N. S. Kurnakov maintained an unflagging interest in the study of salt lakes and deposits and directed the work of his students and co-workers in this field. Following the Great October Socialist Revolution, a series of expeditions for studying the physical chemistry of the salt lakes of the Crimea, Lower Voiga, and other regions of the USSR was organized under his direction. He was especially interested in the Kara-Bogaz-gol gulf of the Caspian Sea, a very rich source of natural salts. In order to understand the crystallization processes which take place in this gulf, N. S. Kurnakov and S. F. Zhemchuzhnyi studied the cosolubility in water of the chlorides and sulfates of sodium and magnesium, the principal components of many saline deposits which originate from sea water. The extent to which the composition of the salt mass in the deposit approached that of the sea water was shown by N. S. Kurnakov to be related to the so-called coefficient of metamorphization (transformation), the ratio of the magnesium sulfate content of the deposit to the magnesium chloride.

In 1916 N. S. Kurnakov published the results of a study on the presence of potassium salts in brines obtained from borings in the neighborhood of Solikamsk. These brines had for centuries served as a source of ordinary salt. Work on deep borings showed the presence of deposits of potassium salts of great industrial importance. The studies of N. S. Kurnakov on mineral salts, ores, and other naturally occurring materials assisted the USSR in developing industries for the production of mineral salts, fertilizers, aluminum, and magnesium.

N. S. Kurnakov generalized the results of his studies of the physical chemical properties of alloys and salt solutions which were of practical importance and developed theoretical rules relating the properties of a system with composition and temperature. In developing and testing these rules he sometimes selected systems which were lacking in practical interest but possessed certain advantages for experimentation and development of new methods of investigation. Certain organic substances proved to be quite useful here since their low melting points made it possible to readily obtain liquid solutions containing any desired amount of either component, while their transparency permitted observation of the crystal structure not only in reflected light, as in the case of metals, but in transmitted light as well. This last fact made it possible to follow the rate of crystallization and the order of appearance of the solid phases. The viscosity method was applied with considerable success to these systems and led N. S. Kurnakov to the discovery of a new type of viscosity isotherm, which showed a maximum corresponding to the composition of a chemical compound which had formed in solution. Similar maxima were then discovered in metal and oxide systems which are less amenable to experimentation. These were designated by N. S. Kurnakov as singular maxima and characterize the compositions of the compounds which have been formed in the liquid phase.

Thus all of those types of melting point diagrams (and diagrams for other properties, as well) which have been found to apply to systems of metals, molten salts, and silicates have also been realized in systems involving organic components. Thus the organic systems are useful models for the study of the relation between properties, composition, and temperature. Many of these organic systems later found practical applications.

The individual chemical substance was then the object of study in organic and inorganic chemistry and, to a certain degree, in physical chemistry as well. Little attention was given to systems or mixtures. On the other hand, D. I. Mendeleev had already called attention to the fact that the study of systems, especially solutions, could make a valuable contribution to the understanding of chemical compounds. The chemical individual enters into such systems as solutions and gaseous mixtures in the course of its preparation and purification. Finally, it is true that most of the materials which find application in technology and daily life (substances such as glass, alloys, foodstuffs) are mixtures rather than pure individuals. On this basis the significance of physical chemical analysis, that branch of theoretical chemistry which was established by N. S. Kurnakov for the study of the relation between system properties, composition and temperature, becomes evident. More than thirty physical properties are now known in which variation with composition, temperature, and pressure is a reflection of physical chemical transformations involving alteration in the number of individuals and phases which are present in a system.

The use of geometrical methods is a characteristic feature of the present day physical chemical analysis. The experimentally established functional relation between property and composition is represented graphically in a composition-property diagram whose geometrical study leads to conclusions concerning the type of interaction between the components of the system, the possible formation of mechanical mixtures, solid solutions, and chemical compounds, and even to information as to the stability of these compounds under the experimental conditions. Thus there is no necessity for the separation and chemical analysis of the compounds which have been produced.

The most important theoretical principle of modern physical chemical analysis is the hypothesis of unity of structure of chemical diagrams. This principle asserts that the form of the diagram is independent of the chemical groups to which the components belong and is fixed by the type of interaction between these components. Thus, the formation of a stable chemical compound in a binary system always leads to the appearance of a maximum on the viscosity diagram regardless whether the components are organic substances, metals, or silicates. N. S. Kurnakov defined the objectives and techniques of physical chemical analysis, formulated its basic principles, and developed the theory of the topology of chemical diagrams, i.e., the theory of those characteristics of graphs representing properties as functions of composition which are related to the general diagram structures. Topology is that branch of geometry which studies those aspects of the form and mutual relations of figures which are independent of dimensions.

One of the techniques of physical chemical analysis is the method of comparison of properties or simultaneous study of the alteration of several characteristics with temperature and concentration. The results are plotted on a single composition-property diagram and then compared. This permits comparison of the isotherms for two or more properties for different types of chemical interaction and facilitates discovery of the interrelationship of these characteristics. Furthermore, the compositions of compounds which are formed in the system and are covered by singular points on the isotherms of two or more characteristics undoubtedly correspond to new individuals.

The work in physical chemical analysis which N. S. Kurnakov and his collaborators carried out in a number of educational and scientific research institutions built up the most extensive school of physical chemists in the USSR; the development of this school was especially marked after the Great October Socialist Revolution. Many of his students and collaborators are now directors of the scientific research work on salts, metals, silicates, and organic systems which is being carried out in the various educational and scientific institutions of the USSR.

The students and collaborators of N. S. Kurnakov continue the development of various phases of physical chemical analysis, studying the processes which occur in natural salt beds, investigating the relation between the properties of alloys, their composition and temperature, and deepening their understanding of liquid and solid solutions through knowledge of properties and structures.

They have a worthy example for emulation in their modest, unassuming teacher, who devoted all of his efforts to the service of science and his native land.

The most important papers of N. S. Kurnakov have been collected in the text "An Introduction to Physical Chemical Analysis," a fourth edition of which appeared in 1940, and in the two volumes of his "Collected Papers" (Volume I appeared in 1938 and Volume II in 1939).

The theoretical papers are included in the "Introduction" while the "Collected Papers" is largely devoted to the experimental studies.

Many papers of N. S. Kurnakov and his students were published in the 27 volumes of the *Izvestiya Instituta (sektora) Fiziko-khimicheskogo Analiza* which appeared from 1920 to 1955.

Volume 14 (1940) of this journal contains articles devoted to the various aspects of the activity of N. S. Kurnakov and his school. The ninth number of Volume 21 of *Uspekhi Khimii* for 1952 is devoted to this same subject.

Various articles devoted to the scientific activity of N. S. Kurnakov are to be found in certain journals of chemistry and general science for 1941.

Interesting biographical information material and information on the scientific activity of N. S. Kurnakov have been collected in the recent book of Yu. I. Solov'ev and O. E. Zvyaginsev, "Nikolai Semenovich Kurnakov, His Life and Work" (Acad. Sci. USSR Press, 1960, p. 207). In addition to footnotes, this text also contains a bibliography of works on N. S. Kurnakov which includes more than 30 titles (pp. 205-206).



## THE ENTHALPIES OF FORMATION AND GRAM-FORMULA VOLUMES OF THE LOWER OXIDES OF VANADIUM

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The calorimetric determination of the enthalpies of formation of the vanadium oxides presents certain difficulties which arise from the fact that recourse must be had to oxidation reactions which fail to go to completion and yield products of indefinite phase composition. This incomplete oxidation of the vanadium oxides is due to the limitation of access of oxygen to the oxidizing material as a result of the formation of surface films of vanadium pentoxide. Naturally, the effect of this factor can be reduced by using a microcalorimeter and thereby diminishing the charge of oxide required for combustion. In this way it has been possible to obtain quite satisfactory results for vanadium oxides of intermediate oxygen content [1].

The present work has been devoted to a study of the lower oxides of vanadium. Working samples were prepared from vanadium iodide which had been rendered frangible by hydrogenation with carefully purified hydrogen, and vanadium trioxide which had been obtained by reducing the analytical grade pentoxide with hydrogen. These two materials were carefully mixed and the mixture then pressed into tablets which were fired for two hours at 1660° in a vacuum resistance furnace with tantalum heating elements. The crucibles were made of "corundum" and showed no signs of reaction with the oxidation products. The composition of the working samples was checked by determining the increase in mass resulting from oxidation to the pentoxide.

The heat of combustion was determined in the vacuum microcalorimeter which has been described earlier in [1]. The experimentally determined heats of combustion of the lower vanadium oxides and the enthalpies of formation calculated from them are given in Table 1. One calorie was assumed equivalent to 4,1840 absolute joules.

Table 2 presents values which various authors have obtained for the enthalpies of formation of the vanadium oxides. Our own values are close to those given in [1, 2]. Values taken from the second of these two references have been included in the tables published by the United States Bureau of Standards [3].

The densities of the vanadium oxides were determined in a vacuum pycnometer, using bromoform as the sealing liquid [6]. The experimentally determined densities of the vanadium oxides and the gram-formula volumes calculated from them are given in Table 3.

The figure shows the variation of enthalpy of formation and gram-formula volume with oxide composition. The dotted line marks the lower limit of the region of homogeneity of vanadium suboxide. It is to be seen that both the gram-formula volume vs composition and the enthalpy of formation vs composition curves show breaks at a composition which corresponds closely to the formula  $\text{VO}_{0.5}$ . Each curve is linear on both sides of the break point.

It is not clear whether the formula  $\text{VO}_{0.50}$  designates a discrete compound or the upper limit of a region of homogeneity which extends to metallic vanadium. In the latter case the situation would be similar to that met in the Ti-O system where there is a region of homogeneity ranging from Ti to  $\text{TiO}_{0.50}$  [7, 8]. A solution

TABLE 1

Enthalpies of Formation of Vanadium Oxides

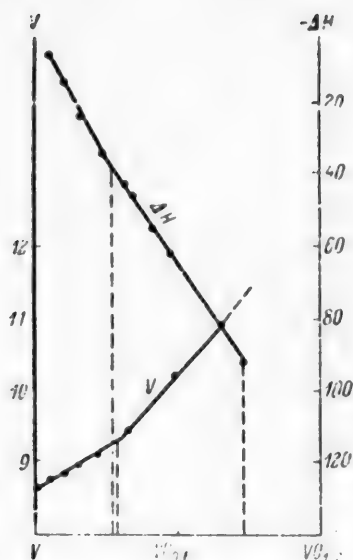
Sample composition	Heat of combustion (kcal/g-formula wt)	$-\Delta H^\circ$ (kcal/g-formula wt)	$-\Delta H^\circ$ (kcal/g-formula wt)
VO <sub>2.50</sub>		186.5 ± 1.5	186.5 ± 1.5
VO <sub>1.112</sub>	{ 69.2 68.2	{ 117.8 118.3	{ 117.8 ± 0.5
VO <sub>0.983</sub>	{ 84.8 84.7	{ 101.7 101.8	{ 101.8 ± 0.2
VO <sub>0.870</sub>	{ 94.2 93.8	{ 92.3 92.7	{ 92.5 ± 0.2
VO <sub>0.770</sub>	{ 107.6 104.4 106.1	{ 78.9 82.1 80.4	{ 80.4 ± 0.8
VO <sub>0.586</sub>	{ 124.7 124.0 125.1	{ 61.6 62.5 61.4	{ 61.9 ± 0.4
VO <sub>0.505</sub>	{ 131.6 130.7 129.8	{ 54.9 55.8 56.7	{ 55.6 ± 0.7
VO <sub>0.473</sub>	{ 133.1 133.3	{ 53.4 53.2	{ 53.3 ± 0.1
VO <sub>0.430</sub>	139.7	46.8	46.8
VO <sub>0.388</sub>	{ 144.7 145.0	{ 41.8 41.5	{ 41.6 ± 0.2
VO <sub>0.288</sub>	{ 151.9 152.6 152.2	{ 34.6 33.9 34.3	{ 34.4 ± 0.5
VO <sub>0.206</sub>	{ 162.3 163.2 161.2	{ 24.2 23.3 25.3	{ 24.3 ± 1.0
VO <sub>0.116</sub>	{ 174.3 172.6	{ 12.3 13.9	{ 13.0 ± 1.0
VO <sub>0.064</sub>	{ 179.6 178.0	{ 6.9 8.5	{ 7.8 ± 0.8

TABLE 2

Enthalpies of Formation of Vanadium Oxides ( $-\Delta H$ , kcal/g-formula wt)

Oxide formula	Published values						Our values
	[1]	[1]	[1]	[1]	[1]	[1]	
VO	08		106 ± 6	100	115	102 ± 1	103 ± 3
V <sub>2</sub> O <sub>3</sub>	320	296 ± 2	300 ± 9	290	320	300 ± 4	
V <sub>2</sub> O <sub>4</sub>	383	342 ± 2	352 ± 14	344	375		
V <sub>2</sub> O <sub>5</sub>	437	373 ± 2	382 ± 12	373	437	376 ± 2	373 ± 3

of this problem will be sought in x-ray studies which we have just undertaken. It is clear that the interval from VO<sub>0.80</sub> to VO<sub>0.30</sub> is a region of two phases. The x-ray diagram of a sample of composition VO<sub>0.86</sub> shows only those lines which are characteristic of vanadium suboxide (NaCl structure), whereas the diagram of a sample of composition VO<sub>0.77</sub> shows not only the lines of a VO<sub>1 ± x</sub> phase but other lines from a new type of phase. The lines of vanadium suboxide become less and less intense as the oxygen content is diminished. A sample of composition VO<sub>0.39</sub> shows only a single line from the VO<sub>1 ± x</sub> phase while the diagram for VO<sub>0.31</sub> shows none of the



Gram-formula volumes ( $v$ ) and enthalpies of formation ( $\Delta H$ ) of the lower oxides of vanadium.

TABLE 3

Densities and Gram-Formula Volumes of the Lower Oxides of Vanadium

Sample composition	Density at 20°, g/cm <sup>3</sup>	Gram-formula volume at 20°, cm <sup>3</sup> /g-formula wt
VO <sub>0.064</sub>	6.11	8.50
VO <sub>0.13</sub>	6.14	8.68
VO <sub>0.21</sub>	6.10	8.90
VO <sub>0.29</sub>	6.06	9.17
VO <sub>0.39</sub>	6.05	9.45
VO <sub>0.59</sub>	5.88	10.27
VO <sub>0.77</sub>	5.94	10.90

vanadium suboxide lines. It follows that the boundary of the two-phase region falls between VO<sub>0.29</sub> and VO<sub>0.39</sub>. In this interval change of the form of the dependence of the enthalpy of formation and the gram-formula volume on composition is observed.

It is noteworthy that the enthalpies of formation and gram-formula volumes of substances falling in the oxygen-lean portion of the region of homogeneity of vanadium suboxide (VO<sub>1.00</sub> - VO<sub>0.86</sub>)<sup>\*</sup> are almost identical with the corresponding values for mixtures of an oxide of the stoichiometric composition VO<sub>1.00</sub> and another oxide of the composition VO<sub>0.33 ± 0.05</sub>. A similar situation has been observed earlier in the case of the lower oxides of titanium [8].

#### SUMMARY

The dependence of enthalpy of formation and gram-formula volume on composition has been established over the interval from V to VO<sub>1.12</sub>.

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\* It will be recalled that the region of homogeneity of vanadium suboxide ranges from VO<sub>0.86</sub> to VO<sub>1.17</sub> [1].

# PHASE DIAGRAMS FOR TERNARY LIQUID SYSTEMS CONTAINING TWO BINARY MISCIBILITY GAPS WITH UPPER CONSOLUTE TEMPERATURES. I

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The most detailed physical chemical analysis of ternary liquid systems containing one homogeneous system and two binary systems showing miscibility gaps with upper consolute temperatures is that which has been made for the case of component interaction in the homogeneous system. It has been established [1-4] that such a homogeneous system (designated as prevailing [5] or predominant [6, 7]) will always play the decisive role in fixing the configuration of the miscibility gap in the composite ternary system. The presence of the chemical compounds of this homogeneous system is manifested by formation of anticlinal, synclinal, or inflectional folds in the partial miscibility region of the ternary system.

In light of this work it would be natural to anticipate that singularities would not appear on the ternary critical point curve, or the saturated solution curves of the miscibility isotherms, of a ternary system which includes a predominant system with normal [8] component relations [9, 10]. The appearance of new experimental material which (as it seems to us) has been in part incorrectly interpreted necessitates a review of this situation [9, 11]. The present work is devoted to a theoretical development and experimental study of phase diagrams for ternary systems which include one binary system showing normal component relations in the homogeneous liquid phase and two binary systems with miscibility gaps.

Let it be supposed that the ternary A-B-C system (Fig. 1) includes one homogeneous binary A-B system whose components are normally related, and two other binary systems, A-C and B-C, which have upper consolute temperatures. The phase diagram for such a ternary system is not fixed by the component relations in the homogeneous system alone but depends on the interaction of the components in the binary gap systems as well. There are three possibilities for this A-B-C system: either 1) neither of the binary gap systems shows component interaction, or 2) one of these systems shows component interaction, or 3) both of these systems show component interaction. Each of these three cases will be considered separately.

Case 1. The homogeneous A-B system will fix the region of partial miscibility in the ternary system at each temperature if there is no component interaction in the gap systems A-C and B-C. The tie lines of isothermal sections of the region of partial miscibility are then directed toward the side of this binary A-B system, and their extensions converge to the C vertex of the concentration triangle. The form of such a region of partial miscibility is shown in Fig. 1a, for a case in which the consolute point in system A-C is higher than the consolute point in system B-C. This figure includes projections of various isothermal sections of the region of partial miscibility onto the composition triangle.

Case 2. The general form of the region of partial miscibility of the ternary system is still similar to that described above if the components of only one of the binary gap systems (assumed to be the B-C system) interact chemically. There will be a single two-phase liquid region in such a ternary system when the temperature is lower than the consolute point in either of the two gap systems. The tie lines of any one isothermal section

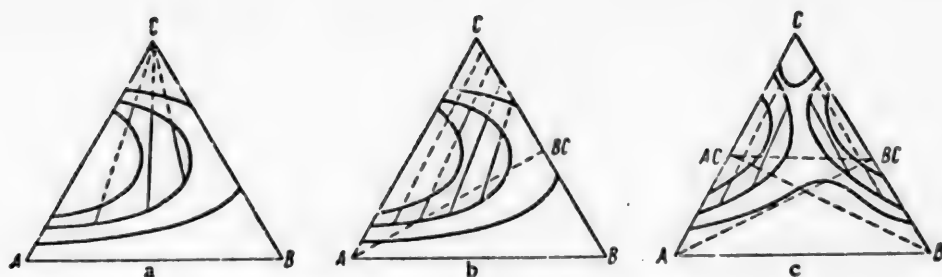


Fig. 1. Possible forms of phase diagrams for ternary liquid systems involving one homogeneous system in which there is no component interaction and two other binary systems with miscibility gaps and upper consolute temperatures. Explanation in text.

will then be continuous and connect points in the A-C and B-C systems representing mutually saturated solutions. A-B will be the predominant binary system under these conditions, and the nodes will be orientated toward this side.

The consolute temperature of the B-C system must be lower than that of the system A-C since B-C involves not only partial miscibility but chemical interaction of the components as well. The region of partial miscibility rests entirely on the A-C side at temperatures above the consolute point in the B-C system and contracts to the consolute point in this A-C system as the temperature is increased. A change will be observed in the predominating system in this temperature interval. The nodes will turn gradually from their original position and move toward the side of the binary B-C system, this effect being the more pronounced the higher the temperature and the greater the active mass of component B. Details of such a ternary phase diagram are shown in Fig. 1b.

Case 3. Component interaction in both of the binary gap systems must invariably produce conditions which favor still other types of interaction in the ternary system. Formation of the compounds AC and BC by chemical interaction between the components of the A-C, B-C systems (Fig. 1c) will give rise to the displacement reaction  $AC + B = BC + A$  in the ternary A-B-C system. This reaction will be represented geometrically by the trapezoid A-AC-BC-B and its diagonals A-BC and B-AC. The point of equilibrium in this displacement reaction may be shifted appreciably in one direction or the other according to the nature of the substances involved and various other factors. An extensive shift of the point of equilibrium in one direction sets up the conditions for stability of a single diagonal. A comparison of the consolute temperatures in the binary gap systems gives a rough idea of the displacement of the point of equilibrium in the case under consideration. The greater the difference of these temperatures, the more pronounced will be the shift of the reaction toward the side of that binary system which has the lower consolute temperature. Such physical chemical interaction of the components of a ternary system cannot alter the geometrical form of the region of partial miscibility or the direction of the tie lines, and the phase diagram must be identical in every respect to that which has been given for the preceding case (Fig. 1b).

It can happen, however, that this reaction is reversible and the point of equilibrium is near the center. This condition gives diagonals of equal stability, so that the binary gap systems predominate to the same degree. The inevitable result is the appearance on the A-C and B-C sides of two separate regions of partial miscibility which expand as the temperature is lowered. Moving toward one another, the isotherms of these regions make contact at their ternary critical points to give a single region of partial miscibility with two saturated solution curves. These latter have the same general form as the individual isotherms and are characterized by a mutual concavity which gradually disappears as the temperature is reduced.

The presence of three predominating boundary systems which compete with one another as the temperature is reduced gives rise to a saddle formation in this type of partial miscibility region (Fig. 1c). The gap systems are predominant at, and somewhat below, their consolute temperatures, and each exerts an homogenizing effect on the opposite region of partial miscibility. The nodes of the individual regions of partial miscibility have a tendency to turn toward these homogenizing systems. The A-C and B-C systems lose their predominating effect as the temperature is reduced and the liquid-phase miscibility gaps of each system increase, the predominating role being then taken over by the A-B system. The nodes in the isothermal sections of the miscibility gaps begin to gradually turn toward this side.

Phase diagrams of this type should be expected, first of all, in ternary systems whose binary gap systems are characterized by component interaction and approximately equal values of the consolute temperatures. It should not be thought, however, that this is a necessary condition. Saddle formation can arise in the region of partial miscibility even with different consolute temperatures in the binary gap systems, provided the equilibrium constant of the reversible reaction tends toward unity at the lower of the two consolute temperatures. It is easily seen that this requires different temperature coefficients of thermal stability for the compounds AC and BC.

We have tested these theoretical considerations on systems which were selected with a view to obtaining the most interesting types of ternary phase diagrams.

## EXPERIMENTAL

Freshly distilled or recrystallized substances whose physical constants were consistent with the values given in the reference literature were employed in this work. The study of liquid phase solubilities was carried out by a visual polythermal method [12] and tie lines were located by the method of sections [13]. Experimentally determined values are not given here, all data being presented graphically in the form of polythermal and isothermal sections of the various ternary phase diagrams.

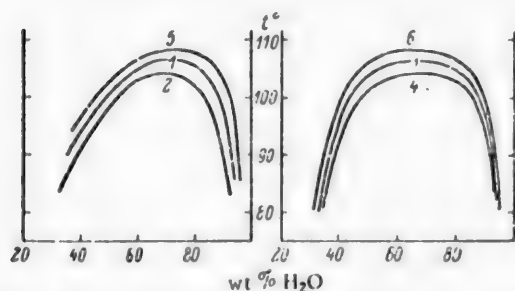


Fig. 2. Polytherms for the ternary system m-nitrobenzoic acid-water-phenylacetic acid. Polytherms for phenylacetic acid in binary mixtures with m-nitrobenzoic acid (weight %): 1) 80; 2) 60; 3) 40; 4) 20; 5) phenylacetic acid-water; 6) m-nitrobenzoic acid-water.

The system m-nitrobenzoic acid-water-phenylacetic acid\* involves the binary systems m-nitrobenzoic acid-water, phenylacetic acid-water, and m-nitrobenzoic acid-phenylacetic acid. Liquid phase solubility in the first of these binary systems has been studied earlier in [12, 14]. The data of these earlier authors show the consolute temperature to be at 107-108.3°. The system phenylacetic acid-water has also been studied [14]. This system shows a region of partial miscibility with an upper consolute temperature of 108°. The literature contains no data on the m-nitrobenzoic acid-phenylacetic acid system. The components of this system have identical chemical functions, and their relations were therefore considered to be close to normal. The binary gap systems have almost identical consolute temperatures, and component interaction takes place in each. It is quite likely that the acid-base interaction between water and the acids is stronger than

the interaction of the acids themselves. All of these facts taken together indicate that the conditions required for the existence of a clearly reversible displacement reaction in the ternary system and a resultant saddle formation in the region of partial miscibility are satisfied. It remains to confirm this conclusion experimentally.

Four polythermal sections were studied in order to establish the temperature and concentration limits of the region of partial miscibility in this ternary system. These sections passed through the water vertex of the composition triangle. Polytherms of these sections are given in Fig. 2 together with polytherms for the binary gap systems. Here the weight percent of water in the binary or ternary heterogeneous mixture has been plotted on the axis of abscissas, and the temperature of passage into a homogeneous solution, on the axis of ordinates. The method of graphic interpolation was used to construct the isotherm sections of the ternary system which are shown in Fig. 3.

The system phenylhydrazine-water-succinonitrile\*\* involves the binary systems phenylhydrazine-water, water-succinonitrile, and phenylhydrazine-succinonitrile. The first of these binary systems has already been studied in [15]. The liquid phase of this system shows a miscibility gap with an upper consolute temperature at 55.2°. It was found that phenylhydrazine interacts with water to form a crystal hydrate which has the formula  $2C_6H_5N_2 \cdot H_2O$  and melts congruently at 25.7°. The miscibility gap of the system lies within the field of this solid phase. Hydration of phenylhydrazine undoubtedly occurs above the critical solution temperature too.

\* This study was carried out with R. A. Naumova.

\*\* This study was carried out with L. I. Denisova.



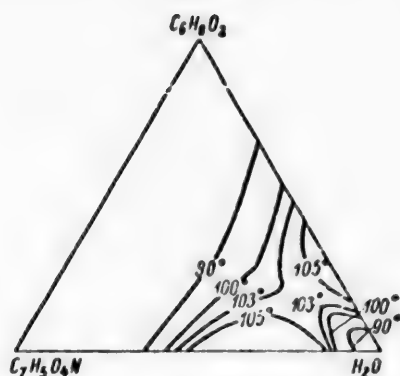


Fig. 3. Isotherms for the system *m*-nitrobenzoic acid–water–phenylacetic acid.

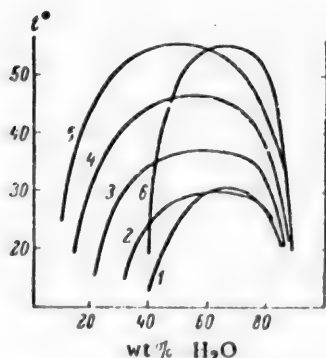


Fig. 4. Polytherms of the ternary system phenylhydrazine–water–succinonitrile. Polytherms of nitrile in binary mixtures with phenylhydrazine (weight %): 1) 19.4; 2) 40.0; 3) 56.7; 4) 78.2; 5) succinonitrile–water; 6) phenylhydrazine–water.

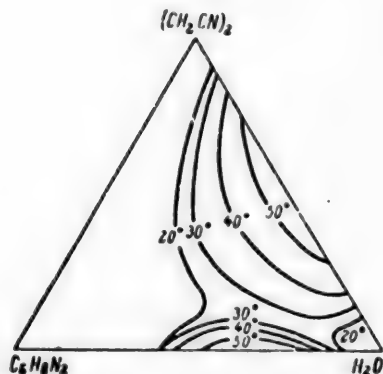


Fig. 5. Isotherms in the system phenylhydrazine–water–succinonitrile.

The solubility of water and succinonitrile has been studied in [16]. The experimental data show that this system has a miscibility gap which lies on the field of nitrile crystallization and has an upper consolute temperature of 55°. The only solid phases detected were those of the components, although it is quite likely that the liquid system contains products from component association. No study was made of the third binary system, phenylhydrazine–succinonitrile, since we have observed that these substances are mutually soluble in all proportions in the liquid state.

Polytherms of four sections were studied in order to establish the temperature and concentration limits of the region of partial miscibility in the ternary system. These sections passed through the water vertex of the composition triangle.

The results are presented in Fig. 4, where the polythermal curves are numbered to correspond with the ordering of the sections, Curve 5 belonging to the region of partial miscibility in the water–succinonitrile system and Curve 6 to the corresponding region in the system phenylhydrazine–water. Isotherms for the ternary system are given in Fig. 5.

The system phenol–water–isobutyric acid\* includes the binary systems phenol–water, isobutyric acid–water, and phenol–isobutyric acid. Liquid phase solubilities in the first of these binary systems have been studied repeatedly [17, 18].

This system shows a miscibility gap with an upper consolute temperature at 66–68°. Similar results have been obtained from studies on the isobutyric acid–water system [19, 20]. Complete intersolubility is met here at temperatures in excess of 24.5°. The components of the third binary system, phenol–isobutyric acid, are completely miscible in the liquid phase. This was assumed to be a typical acid system which would differ from the other two binary systems in being free of component interaction.

The temperature and concentration limits of the region of partial miscibility in the ternary system were determined from a study of three polythermal sections and the solubilities in the binary gap systems. These sections passed through the water vertex of the composition triangle and were directed toward the side of the phenol–isobutyric acid system.

Results of this study of the ternary system are presented graphically in Fig. 6, which also gives polytherms for the binary systems phenol–water and isobutyric acid–water. Figure 7 gives certain isotherms from the region of partial miscibility of the ternary system. The lines for the 35° isotherm are also indicated in this figure. These lines were fixed in the

\* This study was carried out with R. A. Naumova.



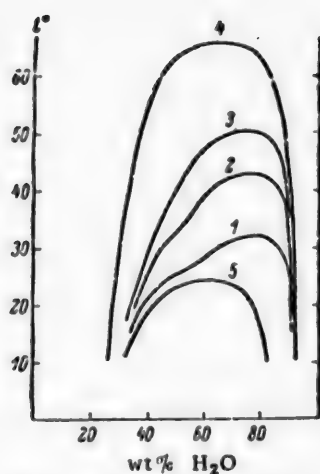


Fig. 6. Polytherms in the ternary system isobutyric acid-water-phenol. Polytherms of phenol in binary mixtures with isobutyric acid (weight %): 1) 20; 2) 45; 3) 70; 4) phenol-water; 5) isobutyric acid-water.

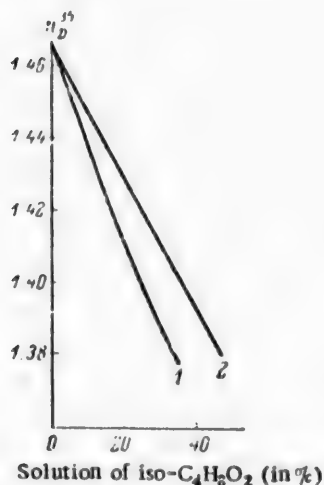


Fig. 8. The relation between the index of refraction of the lower layer from heterogeneous mixtures in the system isobutyric acid-water-phenol and the composition of a 50% isobutyric acid solution. Explanation in text.

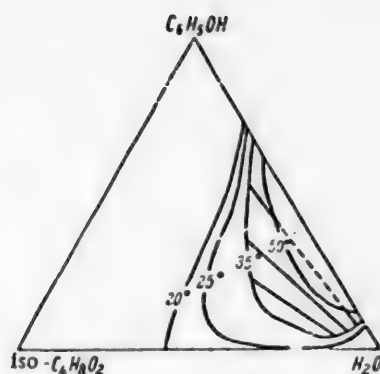


Fig. 7. Isotherms of the system isobutyric acid-water-phenol.

following manner. Various amounts of a 50% aqueous solution of isobutyric acid were added to weighed quantity of binary phenol-water mixtures containing 20 and 40 weight percent phenol. The resulting heterogeneous mixtures were held in a constant temperature bath until liquid phase equilibrium was established, after which a quantity of the lower layer was removed from each and its index of refraction determined. The results are presented by the curve of Fig. 8, which shows the dependence of the index of refraction on the concentration of the isobutyric acid solution. This graph was used to fix the concentrations of the conjugate solutions in the partial miscibility region of the 35° isotherm; concentrations of isobutyric acid corresponding to the measured values of the refractive index being read off of lines 1 and 2. The conjugate phases were obtained by plotting the values thus found on the composition triangle for the system according to section number, drawing straight lines through these points, and extending these lines to intersection with the two branches of the binodal curve.

The system *n*-hexane - aniline - heptane\* includes the binary systems aniline-hexane, aniline-heptane, and hexane-heptane. The first two of these systems have already been investigated [21]; each shows a region of partial miscibility with a consolute temperature in the neighborhood of 69°. The components of the third system, hexane-heptane, are miscible with one another in all proportions. This is the most nearly ideal of all of the binary systems treated here since there is absolutely no associative-dissociative interaction between any of the component molecules.

The method of polythermal sections was used to study liquid phase solubility in the ternary system and led to the isothermal sections of the ternary system which are shown in Fig. 9. The polytherms of the various sections are not included here since they would coincide if plotted in this graph. Our data show upper consolute temperatures of 69° in the aniline-hexane system and 69.5° in the aniline-heptane system.

\* This study was carried out with N. A. Tongshina.

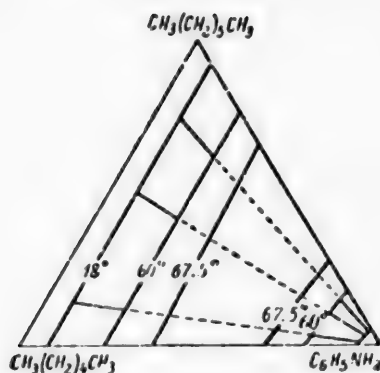


Fig. 9. Isotherms in the system hexane-aniline-heptane and tie lines for the 18° isotherm.

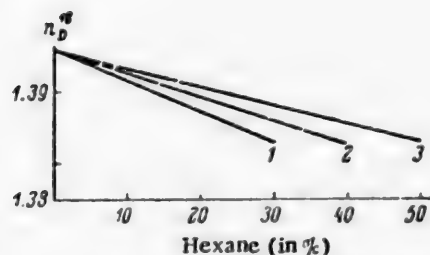


Fig. 10. The relation between the index of refraction of the upper layer from heterogeneous mixtures in the system hexane-aniline-heptane and the hexane content along the isoconcentrates of aniline: 1) 70; 2) 60; 3) 50 mole % aniline.

The method of sections was used to fix the positions of tie lines at 18°. This was done by preparing mixtures from sections corresponding to 70, 60 and 50 weight percent of aniline. Equilibrium was established between the liquid phases, and refractive indices then determined in samples taken from the upper layers. The results are represented graphically in Fig. 10.

#### DISCUSSION OF RESULTS

The results of this study of liquid phase solubility in various ternary systems are in full agreement with the theory. Saddle formation is observed in the region of partial miscibility of each of the first two ternary systems. Separate regions of partial miscibility exist in the system nitrobenzoic acid-water-phenylacetic acid but only over an interval of 4°. The saddle is deeper in the system phenylhydrazine-water-succinonitrile, and separate regions of partial miscibility exist over an interval of 30°. The narrow temperature interval for the existence of separate two-phase liquids in the first of these ternary systems is obviously due to the fact that component interaction results in only an insignificant reduction in the total number of particles. Moreover, the acid hydrates which are formed here probably undergo extensive electrolytic dissociation, whereas the same is not true of the hydrates of phenylhydrazine or succinonitrile.

A saddle can also be formed in the region of partial miscibility of a ternary system when component interaction occurs in the homogeneous binary system. Actual instances of such systems are acetic anhydride-water-benzene [1] and acetic anhydride-water-carbon disulfide [4]. The maximum liquid phase solubility in these systems is located exactly in the quasi-binary sub-systems. The situation was different in our systems. The minimum nodes on the isotherm of the single miscibility gap are not located in the same plane, and their extensions do not pass through the water vertex of the composition triangle but are directed toward either the phenylacetic acid-water or the succinonitrile-water systems. This indicates that the reaction of the ternary systems is displaced toward one of the binary systems.

The results of earlier studies of the systems phenol-water-ammonium rhodanide [9], diphenylamine-sulfur-*B*-naphthylamine [11], and salicylic acid-water-anthranilic acid [11] become clear in the light of our own investigations. The form of the miscibility gaps in these systems is not due to chemical interaction of the components of the homogeneous binary system (ammonium rhodanide-water, diphenylamine-*B*-naphthylamine, or salicylic acid-anthranilic acid), as claimed by these various authors, but to the fact that component interaction in the gap binary systems leads to a reversible displacement reaction.

A displacement reaction also occurs in the ternary system isobutyric acid-water-phenol. This reaction is, however, definitely displaced toward the side of the binary system isobutyric acid-water, where the acid-base interaction is more pronounced than in the phenol-water system. The result is that there is a single miscibility gap, and the curve of ternary critical points does not pass through a saddle point. Two of the binary gap systems are capable of entering into competition with the homogeneous system, but only one of these is predominant. The position of the tie lines makes this situation quite obvious.

The ternary system hexane-aniline-heptane is specially interesting. This is similar to the ternary systems which have been considered above in that the consolute temperatures in its binary gap systems are almost identical. Nevertheless, its solubility isotherms do not show a saddle formation but are ideal straight lines. Situations of this kind arise with normal component relations in the homogeneous binary system and no component interaction in the gap binary systems. The homogeneous hexane-heptane system is the only one of the binary systems which is predominant. Study shows the tie lines of the 18° isotherm to fan out toward the side of this homogeneous system while their extensions in the opposite direction pass through the aniline vertex of the composition triangle. The geometry of the isothermal sections of the miscibility gap is such that the nodes would be similarly directed at other temperatures as well.

#### SUMMARY

1. Study has been made of the possible types of phase diagrams for ternary liquid systems containing two binary miscibility gaps with upper consolute temperatures. It has been shown theoretically that two types of diagram are possible when there is no component interaction in the third, homogeneous, binary system.

2. These conclusions were tested by a study of the miscibility gaps in the ternary systems m-nitrobenzoic acid-water-phenylacetic acid, phenylhydrazine-water-succinonitrile, phenol-water-isobutyric acid, and hexane-aniline-heptane. The experimental results were in full agreement with the theory.

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## CONDUCTIVITY, VISCOSITY, AND DENSITY MEASUREMENTS IN THE SYSTEMS $\text{SnCl}_4\text{-C}_2\text{H}_5\text{OH-C}_6\text{H}_6$ AND $\text{SnCl}_4\text{-C}_3\text{H}_7\text{OH-C}_6\text{H}_6$

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The interaction of the stannic halides and alcohols has been investigated repeatedly [1-13]. It has been shown that one molecule of stannic halide will unite with two alcohol molecules [1-7] and there is evidence of the existence of other compounds such as  $\text{SnCl}_4 \cdot 3\text{ROH}$  [7],  $\text{SnCl}_4 \cdot 4\text{ROH}$  [8, 9] and  $\text{SnCl}_4 \cdot 5\text{ROH}$  [9] which are still richer in alcohol. The measurements of Wertyporoch and Altmann [13] have proven the conductivity of solutions of stannic chloride in methyl and ethyl alcohols to be rather high ( $1 \cdot 10^{-3} \text{ ohm}^{-1} \text{ cm}^{-1}$ ). These authors ascribe the electrical conductivity of such solutions to the formation of complex compounds. Conductivity, viscosity, and density measurements have proven that the conductivity of the systems  $\text{SnCl}_4\text{-RCOOH}$ ,  $\text{SnBr}_4\text{-RCOOH}$  and  $\text{SnCl}_4\text{-RCOOR'}$  is due to the formation of the compounds  $\text{SnX}_4 \cdot 3\text{A}$  and  $\text{SnX}_4 \cdot 4\text{A}$  [14-18]. Ion transfer studies have established the mode of electrolytic dissociation of these compounds and shown that the organic component is a constituent of both cation and anion [10, 11]. (Arguing by analogy, it could be assumed that compounds  $\text{SnX}_4 \cdot 3\text{ROH}$  and  $\text{SnX}_4 \cdot 4\text{ROH}$  would be formed in  $\text{SnX}_4\text{-ROH}$  systems, where they would dissociate to render these systems conducting.

The present work is a report of conductivity, viscosity, and density measurements in the systems  $\text{SnCl}_4\text{-C}_2\text{H}_5\text{OH-C}_6\text{H}_6$  and  $\text{SnCl}_4\text{-C}_3\text{H}_7\text{OH-C}_6\text{H}_6$ .

### EXPERIMENTAL

Stannic chloride of "pure" grade was repeatedly redistilled over  $\text{P}_2\text{O}_5$  in a distillation apparatus equipped with a fractionating column. The fraction boiling at  $109^\circ$  under a pressure of 694.5 mm was distilled into ampules in a special apparatus [19]. This apparatus had been connected for several days to a bulb containing  $\text{P}_2\text{O}_5$  in order to remove the moisture of the air. The benzene was purified by the usual methods and had a melting point of  $5.5^\circ$ . The ethyl and propyl alcohols were dehydrated with  $\text{CaO}$ , subjected to further drying over metallic sodium, and fractionated. The ethyl alcohol boiled at  $75.9^\circ$  (685.5 mm); its characteristic constants were  $d^{20}_4$  0.7898,  $n^{20.5}_D$  1.3610, while the literature values are  $d^{20}_4$  0.7894,  $n^{20.5}_D$  1.3610. The propyl alcohol boiled at  $95.3^\circ$  (699.8 mm); its characteristic constants were  $d^{20}_4$  0.8039,  $n^{20}_D$  1.3854, while the literature values are  $d^{20}_4$  0.80355,  $n^{20}_D$  1.38533. The purified alcohols were stored in sealed ampules. The experimental techniques have been described earlier in [20]. Preparation of the mixtures and loading of the apparatus for the various measurements were carried out in a special  $\text{P}_2\text{O}_5$ -dried hood from which the external air was excluded.

1. The electrical conductivity, viscosity, and density were measured in the  $\text{SnCl}_4\text{-C}_2\text{H}_5\text{OH}$  system at two temperatures ( $40$  and  $60^\circ$ ) and at two dilutions (50 and 70 mole %  $\text{C}_6\text{H}_6$ ). The results of these measurements are shown in Table 1. Composition-property diagrams are given in Fig. 1. This figure shows that the isothermal viscosity curves corresponding to various concentrations of  $\text{C}_6\text{H}_6$  pass through a maximum at 30-33 mole percent  $\text{SnCl}_4$ . The viscosity falls as the temperature is increased or the benzene content is raised, but the

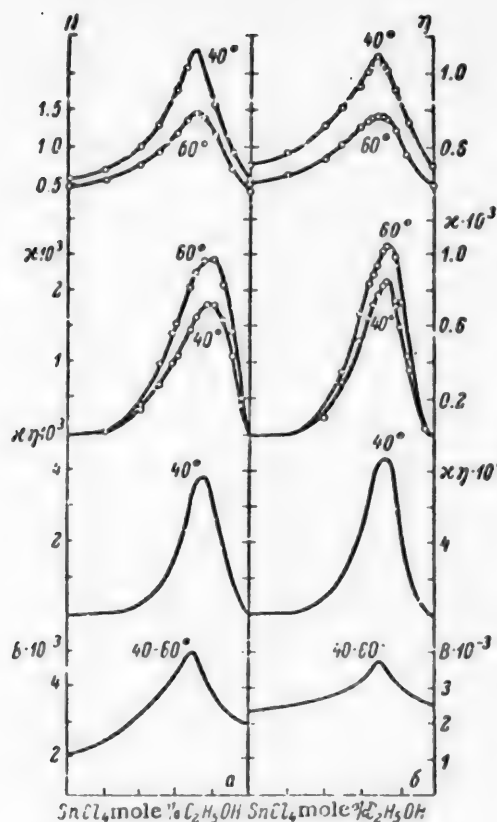


Fig. 1.

Fig. 1. Property-composition diagrams for the system  $\text{SnCl}_4\text{-C}_2\text{H}_5\text{OH-C}_6\text{H}_6$ : a) curves of constant concentration, 50 mole %  $\text{C}_6\text{H}_6$ ; b) curves of constant concentration, 70 mole %  $\text{C}_6\text{H}_6$ .

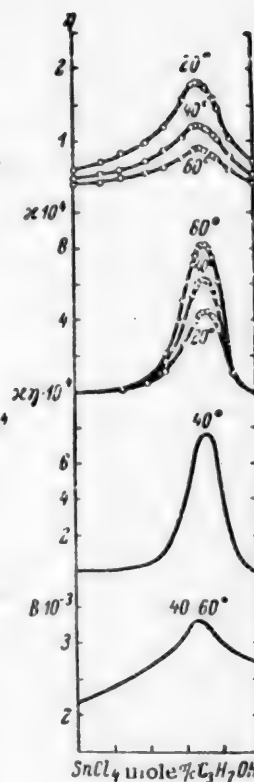


Fig. 2.

Fig. 2. Property-composition diagrams for the system  $\text{SnCl}_4\text{-C}_3\text{H}_7\text{OH-C}_6\text{H}_6$  (constant concentration curves, 70 mole %  $\text{C}_6\text{H}_6$ ).

position of the maximum remains unchanged. The form of these curves and the value of the constant  $B$  ( $\eta = A e^{B/RT}$ ) both point to the formation of  $\text{SnCl}_4 \cdot 2\text{C}_2\text{H}_5\text{OH}$ , a compound which has been described earlier [1-6].

The conductivity of solutions of stannic chloride in ethyl alcohol is rather high ( $\kappa_{50} = 4 \cdot 10^{-3} \text{ ohm}^{-1} \text{ cm}^{-1}$ ). The specific conductivity increases as ethyl alcohol is added to the stannic chloride, quite slowly up to 70 mole percent  $\text{SnCl}_4$  and then rapidly, up to a maximum at 22-26 mole percent  $\text{SnCl}_4$ ; beyond this point the conductivity drops off sharply. The maximum in the specific conductivity is displaced slightly in the direction of the alcohol by an increase in the temperature. The general form of these isotherms remains unaltered when viscosity corrections are introduced. The maximum on the corrected conductivity curve comes at 25 mole percent  $\text{SnCl}_4$  which marks the composition of that 1:3 compound which is responsible for the conductivity shown by the system.

Thus the conductivity, viscosity, and density measurements in the  $\text{SnCl}_4\text{-C}_2\text{H}_5\text{OH}$  system were extended to cover the entire concentration range by transferring the system into a solvent-benzene. These measurements confirmed the existence of the compound  $\text{SnCl}_4 \cdot 2\text{C}_2\text{H}_5\text{OH}$  and disclosed the formation of a second compound, of the composition  $\text{SnCl}_4 \cdot 3\text{C}_2\text{H}_5\text{OH}$ .

2. The conductivity, viscosity, and density were measured in the  $\text{SnCl}_4\text{-C}_3\text{H}_7\text{OH}$  system at three temperatures (20, 40, and 60°) and at a single dilution (70 mole %  $\text{C}_6\text{H}_6$ ). The results of these measurements are presented in Table 2 and Fig. 2.

TABLE 1

Properties of the System  $\text{SnCl}_4\text{-C}_2\text{H}_5\text{OH-C}_6\text{H}_6$

Mole % $\text{SnCl}_4$ (without allowance for solvent)	Viscosity (in centi- poise)		Density (g/cm <sup>3</sup> )		$\kappa \cdot 10^3$ (ohm <sup>-1</sup> cm <sup>-1</sup> )	
	40°	60°	40°	60°	40°	60°
Isoconcentrate, 50 mole % $\text{C}_6\text{H}_6$						
0.00	0.5326	0.3957	0.8230	0.8032	—	—
4.99	—	—	—	—	0.364	0.449
9.98	0.9141	0.6768	0.9663	0.9455	1.06	1.40
15.01	—	—	—	—	1.56	2.04
19.99	1.540	1.148	1.1045	1.0835	1.77	2.40
24.96	crystallized	1.284	1.1683	1.1448	1.79	2.37
29.94		1.437	1.2115	1.1877	1.61	2.24
33.26	crystallized	—	—	—	1.43	2.04
35.00	2.052	1.239	—	—	—	—
39.95	—	—	—	—	1.07	1.49
40.00	1.766	1.182	1.2961	1.2743	—	—
42.86	—	—	—	—	0.973	1.38
50.09	1.283	0.9226	1.3636	1.3373	0.683	0.950
50.51	—	—	—	—	0.698	0.955
60.26	1.015	0.7595	1.4247	1.3951	0.508	0.898
79.56	0.6824	0.5413	1.5145	1.4813	0.0199	0.0256
100.00	0.5435	0.4442	1.5958	1.5598	—	—
Isoconcentrate, 70 mole % $\text{C}_6\text{H}_6$						
0.00	0.4812	0.3688	0.8381	0.8174	—	—
5.00	—	—	—	—	0.0239	0.0210
13.00	0.7265	0.5532	0.9404	0.9196	0.346	0.417
17.75	—	—	—	—	0.593	0.728
20.02	0.9119	0.7836	0.9938	0.9694	0.701	0.986
24.95	1.028	0.7467	1.0323	1.0073	0.837	1.05
27.24	1.050	—	—	—	0.822	—
27.13	1.050	0.7601	—	—	0.826	1.02
30.00	1.090	0.7639	1.0616	1.0382	0.779	0.939
33.33	1.031	0.7457	—	—	0.705	0.894
35.00	1.003	0.7349	—	—	0.635	0.837
39.76	0.9364	0.7076	1.1085	1.0848	0.509	0.664
50.05	0.8081	0.6096	1.1519	1.1266	0.281	0.338
59.84	0.7064	0.5365	1.1895	1.1635	0.0975	0.0993
79.70	0.5685	0.4466	1.2585	1.2306	0.00256	0.00355
100.00	0.4846	0.3924	1.3229	1.2925	—	—

Figure 2 shows that the viscosity isotherms in the  $\text{SnCl}_4\text{-C}_3\text{H}_7\text{OH}$  system pass through a maximum at a composition of 32-30 mole percent of  $\text{SnCl}_4$ ; this would correspond to the formation of a compound  $\text{SnCl}_4 \cdot 2\text{C}_3\text{H}_7\text{OH}$ . The maximum is displaced slightly toward the propyl alcohol with increasing temperature. The formation of the compound  $\text{SnCl}_4 \cdot 2\text{C}_3\text{H}_7\text{OH}$  is also indicated by the fact the curve showing the dependence of  $\eta$  on composition passes through a maximum at 33 mole percent  $\text{SnCl}_4$ . The  $\text{SnCl}_4\text{-C}_3\text{H}_7\text{OH}$  system resembles the  $\text{SnCl}_4\text{-C}_2\text{H}_5\text{OH}$  system in showing high electrical conductivity. The specific conductivity isotherms pass through a maximum at 25 mole percent  $\text{SnCl}_4$ . The specific conductivity increases with rising temperature and the maximum moves toward the propyl alcohol. The corrected conductivity isotherms also pass through a maximum at 26-27 mole percent  $\text{SnCl}_4$ . The position of this maximum points to the formation of the compound  $\text{SnCl}_4 \cdot 3\text{C}_3\text{H}_7\text{OH}$ .

Thus it can be concluded that the compounds  $\text{SnCl}_4 \cdot 2\text{C}_3\text{H}_7\text{OH}$  and  $\text{SnCl}_4 \cdot 3\text{C}_3\text{H}_7\text{OH}$  are formed in the  $\text{SnCl}_4\text{-C}_3\text{H}_7\text{OH}$  system.

#### DISCUSSION OF RESULTS

Physical chemical analysis of the liquid phases of the  $\text{SnCl}_4\text{-C}_2\text{H}_5\text{OH-C}_6\text{H}_6$  and  $\text{SnCl}_4\text{-C}_3\text{H}_7\text{OH-C}_6\text{H}_6$  systems has shown that complex formation leads to compounds of the general formula  $\text{SnCl}_4 \cdot 2\text{ROH}$  and  $\text{SnCl}_4 \cdot 3\text{ROH}$  in each.



TABLE 2

Properties of the System  $\text{SnCl}_4\text{-C}_2\text{H}_5\text{OH-C}_6\text{H}_6$  (isoconcentrate, 70 mole %  $\text{C}_6\text{H}_6$ )

Mole % $\text{SnCl}_4$	Viscosity (in centipoise)			Density ( $\text{g/cm}^3$ )			$\kappa \cdot 10^2$ ( $\text{ohm}^{-1}\text{cm}^{-1}$ )		
	20°	40°	60°	20°	40°	60°	20°	40°	60°
0.00	0.7259	0.5283	0.4058	0.8571	0.8371	0.8176	—	—	—
12.07	1.039	0.7522	0.5711	0.9480	0.9265	0.9070	0.106	0.121	0.143
20.24	1.462	1.007	0.7574	—	—	—	0.355	0.470	0.611
22.27	1.561	1.071	0.7774	—	—	—	0.410	0.564	0.743
24.92	1.655	1.127	0.8450	1.0389	1.0174	0.9967	0.441	0.614	0.803
25.01	1.655	1.125	0.8334	—	—	—	0.446	0.625	0.818
27.32	1.730	1.140	0.8576	—	—	—	0.464	0.655	0.859
27.51	1.740	1.172	0.8639	—	—	—	—	—	—
29.78	1.795	1.199	0.8955	—	—	—	0.446	0.638	0.860
30.06	1.797	1.201	0.8748	—	—	—	0.449	0.642	0.836
31.47	1.807	1.199	0.8653	—	—	—	0.432	0.615	0.791
32.90	1.783	1.183	0.8609	1.0876	1.0634	1.0412	0.398	0.579	0.758
33.67	1.737	1.155	0.8489	—	—	—	0.376	0.544	0.705
39.83	1.546	1.047	0.7638	—	—	—	0.266	0.391	0.500
49.81	1.198	0.8546	0.6539	1.1642	1.1391	1.1151	0.119	0.168	0.201
60.24	0.9979	0.7190	0.5597	1.2109	1.1840	1.1592	0.0415	0.0478	0.0527
74.19	0.8187	0.6110	0.4812	1.2631	1.2345	1.2076	0.00492	0.00429	0.00407
85.27	0.7158	0.5455	0.4372	1.3055	1.2748	1.2456	—	—	—
100.00	0.6136	0.4846	0.3924	1.3548	1.3229	1.2925	—	—	—

TABLE 3

Specific Conductivity of Solutions of  $\text{SnCl}_4$  in Ethyl Alcohol

Our data		Data of Rogov [9]	
mole % $\text{SnCl}_4$	$\kappa \cdot 10^3$	mole % $\text{SnCl}_4$	$\kappa \cdot 10^3$
1.25	0.671	1.15	1.32
2.08	1.15	2.32	2.14
3.52	2.00	3.00	2.65
5.21	2.99	4.21	3.34
7.66	3.94	5.03	3.82
10.24	4.17	6.81	5.25
12.64	3.74	7.42	5.68
15.10	3.13	7.94	5.96
15.35	2.92	8.82	6.21
		9.57	6.47
		12.23	6.53
		13.67	6.32
		15.72	5.50
		17.70	5.41
		20.00	5.38
		21.70	5.42
		24.9	5.62

S. V. Rogov [9] has measured the conductivity, viscosity, and density of solutions of stannic chloride in ethyl alcohol, working over the range of concentrations from 1.15 to 24.9 mole %  $\text{SnCl}_4$ , and has concluded that a compound of the composition  $\text{SnCl}_4 \cdot 4\text{C}_2\text{H}_5\text{OH}$  is formed here. In his opinion, the existence of this compound gives rise to a singular point in all property-composition diagrams.

We decided to check Rogov's data since our own gave no indication of the existence of a 1:4 compound. A comparison of our measurements of the specific conductivity with those of Rogov is given in Fig. 3 and in Table 3. Our data indicates that the conductivity of the solution of stannic chloride in ethyl alcohol is less than that reported by Rogov by a factor 1:1.5. We were, moreover, unable to make measurements over the concentration interval from 15 to 25 mole %  $\text{SnCl}_4$  since crystallization invariably occurred in this range.



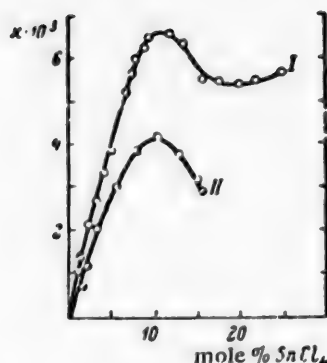


Fig. 3. Specific conductivity in the binary system  $\text{SnCl}_4\text{-C}_2\text{H}_5\text{OH}$ : I) data of Rogov; II) our data.

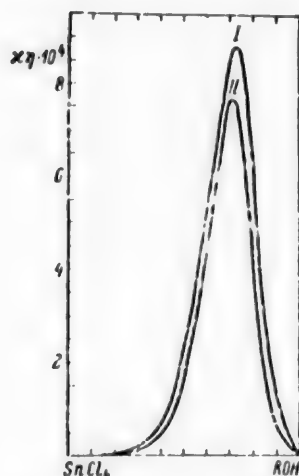


Fig. 4. Corrected conductivities in the  $\text{SnCl}_4\text{-C}_2\text{H}_5\text{OH}$  (I) and  $\text{SnCl}_4\text{-C}_3\text{H}_7\text{OH}$  (II) systems (isoconcentrate, 70 mole %  $\text{C}_6\text{H}_6$ ).

This comparison makes it clear that we were unable to reproduce Rogov's measurements on the electrical conductivity. It also seems doubtful to us that singular points occur on the property-composition diagrams developed by Rogov. Singular points corresponding to a compound of the composition  $\text{SnCl}_4 \cdot 4\text{C}_2\text{H}_5\text{OH}$  would certainly be detected on the property-composition diagrams for the ternary system  $\text{SnCl}_4\text{-C}_2\text{H}_5\text{OH-C}_6\text{H}_6$ , if they existed at all. It can be seen that no such singular points appear on the viscosity and conductivity diagrams which we have developed. In actuality, such points are not even to be found on the Rogov diagrams.

A comparison of the corrected electrical conductivities in the systems  $\text{SnCl}_4\text{-C}_2\text{H}_5\text{OH-C}_6\text{H}_6$  (I) and  $\text{SnCl}_4\text{-C}_3\text{H}_7\text{OH-C}_6\text{H}_6$  (II) is made in Fig. 4. Curve I of this figure lies above Curve II, and the corrected conductivity is therefore higher in the  $\text{SnCl}_4\text{-C}_2\text{H}_5\text{OH-C}_6\text{H}_6$  system than in the  $\text{SnCl}_4\text{-C}_3\text{H}_7\text{OH-C}_6\text{H}_6$  system. This indicates a diminution in the degree of chemical interaction in passing from  $\text{C}_2\text{H}_5\text{OH}$  to  $\text{C}_3\text{H}_7\text{OH}$ . In other words, ethyl alcohol is oxidized more readily than propyl alcohol under the action of the highly charged  $\text{Sn}^{+4}$  ions.

We have observed a similar diminution in the degree of acid-base interaction with increasing length of acid or alcohol radical in the case of other carboxylic acids [15, 16] and their esters [17, 18].

#### SUMMARY

1. Conductivity, viscosity, and density have been studied in the  $\text{SnCl}_4\text{-C}_2\text{H}_5\text{OH-C}_6\text{H}_6$  system at 40 and 60° with 50 and 70 mole % added  $\text{C}_6\text{H}_6$ ; these same characteristics have been studied in the  $\text{SnCl}_4\text{-C}_3\text{H}_7\text{OH-C}_6\text{H}_6$  system at 20, 40, and 60° with 70 mole % added  $\text{C}_6\text{H}_6$ .

2. It has been shown that the viscosity isotherms indicate the formation of the compounds  $\text{SnCl}_4 \cdot 2\text{C}_2\text{H}_5\text{OH}$  and  $\text{SnCl}_4 \cdot 2\text{C}_3\text{H}_7\text{OH}$ .

3. It has also been concluded that the compounds  $\text{SnCl}_4 \cdot 3\text{C}_2\text{H}_5\text{OH}$  and  $\text{SnCl}_4 \cdot 3\text{C}_3\text{H}_7\text{OH}$  are formed in these systems. We believe these compounds to be responsible for the electrical conductivity.

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## DETERMINATION OF THE MOLECULAR WEIGHTS OF SOLID NORMAL PARAFFINS

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We have tested the cryoscopic method for determining molecular weights by using it to obtain molecular weights of normal paraffin hydrocarbons whose molecules contain 26 or more carbon atoms. Concordant results did not always follow from parallel experiments with different solvents (benzene in the one case and naphthalene in the other). These deviations between the experimentally determined and the calculated molecular weights were due to the limited solubilities of the pure high-molecular normal paraffins in both benzene and naphthalene, so that the concentration of dissolved hydrocarbon was low and the freezing point depression infinitesimally small. The dissolved hydrocarbon would often begin to crystallize out much earlier than the solvent, even in cases where the hydrocarbon concentration was satisfactorily high. These two factors were responsible for a high experimental error.

The pronounced solvent action of camphor led us to employ the Rast method [1, 2] for determining the molecular weights of individual solid paraffins. The results did not agree with theoretical calculations. This lack of agreement was due to the fact that the melt obtained by fusing camphor and the working material together in a capillary was not homogeneous.

Karlsohn [3] has retained the principle of the Rast method but so modified the technique that it is the initial freezing point which is observed rather than the melting point, the preliminary fusion of the camphor and the working substance and the measurement of the freezing temperature being carried out on the entire charge in a single tube. Such operating conditions rather effectively eliminate the possibility of non-homogeneity in the melt. Aluisse [4] later applied this method to the determination of the molecular weights of the deeply colored products resulting from condensation of organic compounds, using an apparatus of his own design.

We have tested this modified version of the Rast method. It was found that the correct value of the molecular weight could be obtained from freezing point depression measurements which were carried out in the course of a single day. The freezing point depression of a given charge was lower on the second and on subsequent days than it had been on the first, and the molecular weight was proportionately higher. This effect was observed in a number of pure normal paraffin hydrocarbons of high molecular weight (containing more than 26 carbons per molecule) and in fractions of solid petroleum paraffins. It was also found that the experimentally determined and calculated molecular weights would still agree if the charge of camphor and hydrocarbon had not been heated on the preceding day. A more detailed study of these effects was not undertaken.

### EXPERIMENTAL

The synthetic camphor (racemate) which was used as solvent had been twice recrystallized from alcohol and then resublimed; its melting point was 177.7°.

The cryoscopic constant of this camphor was obtained with *n*-dichlorobenzene whose purity had been checked thermographically; its value proved to be 40.27.

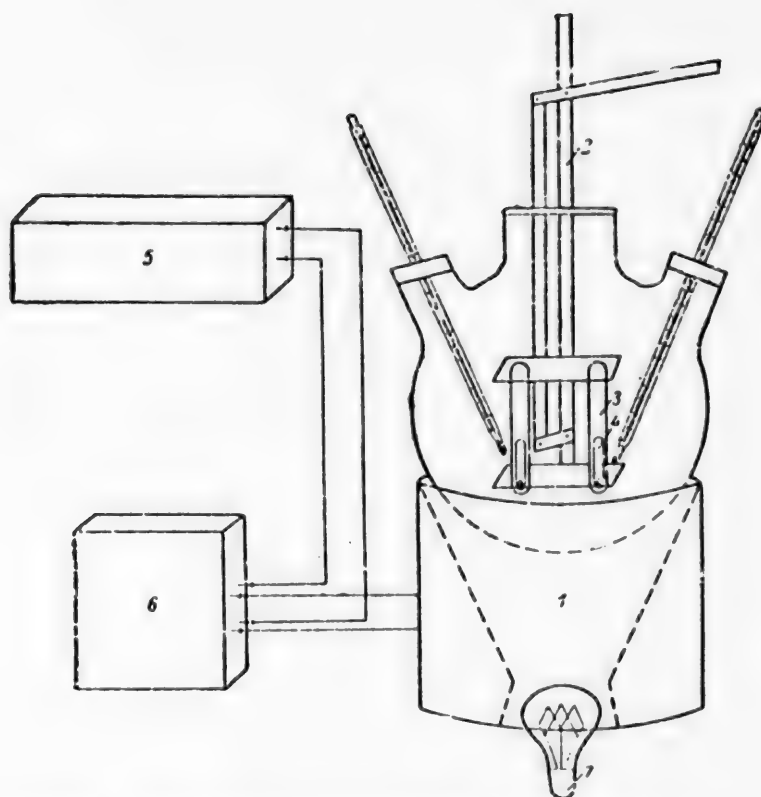


Diagram of apparatus for molecular weight determinations: 1) Electrical heater; 2) stirrer; 3) ampule; 4) capsule; 5) voltage stabilizer; 6) automatic transformer; 7) viewing lamp.

**Experimental procedure.** Eight to ten milligrams of the working material was mixed with ten times this weight of pure camphor in a glass ampule. A capsule containing lead shot was then introduced into the ampule and the latter sealed. The same operations were carried out on a second ampule which contained camphor alone. This arrangement assured the formation of a very thin liquid film between the ampule and the capsule so that the appearance of the first crystals during reduction of the bath temperature could be detected readily.

Both ampoules were firmly screwed onto a special stirrer which was inserted in a three-neck flask containing glycerine. The crystallization temperature was measured on two 0.2° thermometers, each placed as closely as possible to one of the ampoules. The bath was set into a covered conical-form electrical heater from which the lower portion of the cone had been cut away. An electric lamp was inserted into this lower opening to assure good visibility of the crystallizing material.

The temperature was regulated by an automatic laboratory transformer. A sketch of this apparatus is given in the figure. The bath temperature was maintained 5-10° above the melting point of the camphor. The contents of the ampule were mixed for 10-15 minutes prior to beginning the experiment and the heaters then turned on. The temperature at which the first crystals appeared was noted as the initial crystallization point. The freezing point of the pure camphor was measured at the same time. Each determination required 40-50 minutes and was repeated several times. For simplicity, only three or four measured values of the depression are given in the table. The molecular weight was calculated from the well-known equation:

$$M = \frac{K \cdot 1000 \cdot A}{\Delta T \cdot L}$$

In which K is the cryoscopic constant, A is the weight of working material,  $\Delta T$  is the freezing point depression, and L is the weight of the solvent.

Results from Molecular Weight Determinations on Individual Hydrocarbons

Hydrocarbon	Formula	Weight of working material, g	Weight of camphor, g	Freezing point depression	Molecular weight	
					experimentally determined	calculated
n-Docosane*	$C_{22}H_{46}$	0.0103	0.1130	11.8, 11.8, 11.4*	311, 311, 322	310
n-Hexacosane	$C_{26}H_{54}$	0.0111	0.0896	14, 13.4, 13.6	356, 380, 366	336
n-Triacontane*	$C_{30}H_{62}$	0.0910	0.1021	7.9, 8.6, 8.5	454, 417, 422	422
n-Dotriacontane*	$C_{32}H_{66}$	0.0100	0.0981	9.0, 8.8, 8.8	456, 466, 466	450
n-Tetracontane	$C_{34}H_{70}$	0.0073	0.0915	7.4, 7.5, 7.5	463, 470, 470	478
Octadecylcyclohexane**	$C_{24}H_{46}$	0.0141	0.1005	16.6, 16.8, 16.9	334, 340, 336	336
Tricyclohexylindane***	$C_{27}H_{40}$	0.0139	0.1105	14.0, 14.0, 13.9	364, 364, 360	364
Dicyclopentyl-p-xylene***	$C_{18}H_{22}$	0.0096	0.1006	17.0, 17.0, 16.9	248, 248, 249	241
Phenanthrene	$C_{14}H_{10}$	0.0113	0.0961	27.0, 27.0, 26.6	173, 173, 176	178
p-Dichlorobenzene	$C_6H_4Cl_2$	0.0110	0.0992	31.6, 30.8, 30.4	141.3, 144.9, 146.8	246.9

\* These normal paraffin hydrocarbons were synthesized by E. M. Terent'eva.

\*\* This hydrocarbon was furnished by V. V. Shekeldin.

\*\*\* These hydrocarbons were furnished by E. S. Pokrovska.

Data from determinations of the molecular weights of a number of individual hydrocarbons are given in the table. The molecular weights of narrow fractions (M ranging from 260 to 770) of petroleum paraffins which had been separated by molecular distillation could be reproduced with an accuracy of 2-3%.

#### SUMMARY

A modification of the Rast method has been tested and gave entirely satisfactory values for the molecular weights of solid high-molecular hydrocarbons.

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## AROMATIC HYDROCARBONS

### XVI. AROMATIZATION OF HALOGEN SUBSTITUTED TETRAHYDROPHTHALIC ACIDS (ADDUCTS OF DIENE SYNTHESIS) UNDER THE ACTION OF PHOSPHORUS PENTOXIDE

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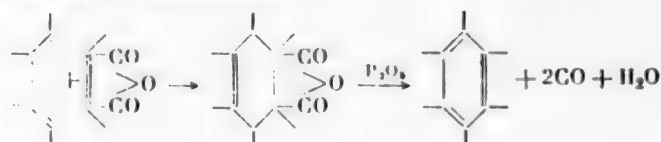
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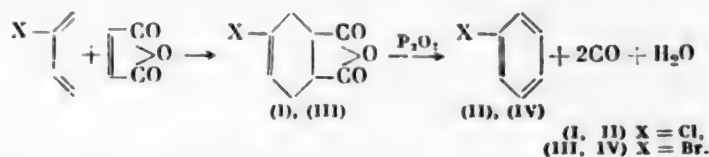
November, 1960

Original article submitted December 17, 1959

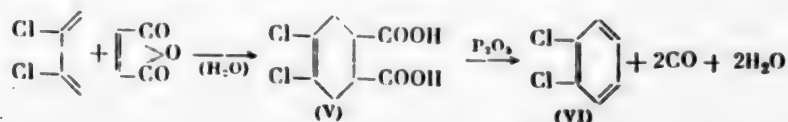
The aromatization reaction of tetrahydrophthalic acids and their anhydrides (adducts of diene hydrocarbons with maleic anhydride, its homologs and cyclic analogs) under the action of phosphorus pentoxide has been used by us until now for the preparation of hydrocarbons with a benzene ring (of the benzene, tetralin, indan, and phenanthrene series [1]), but not of their derivatives.



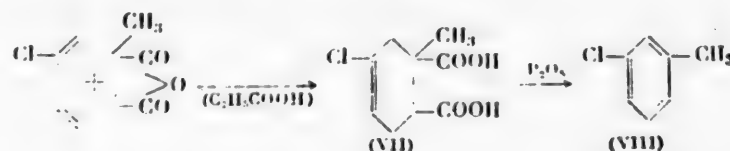
In the present work we show that this reaction is given by halogen-substituted tetrahydrophthalic acids and their anhydrides — the adducts of halogen-substituted dienes with maleic and methylmaleic anhydrides. Thus, 4-chloro-1,2,3,6-tetrahydrophthalic anhydride (I) (the adduct of chloroprene and maleic anhydride) upon heating with phosphorus pentoxide is converted to chlorobenzene (II) (yield, 45%) with loss of water and two molecules of carbon monoxide. An analogous reaction with 4-bromo-1,2,3,6-tetrahydrophthalic acid (III, obtained by hydrolyzing the adduct of bromoprene with maleic anhydride) led to bromobenzene (IV; yield 42%).



4,5-Dichloro-1,2,3,6-tetrahydrophthalic acid (V, from the adduct of 2,3-dichloro-1,3-butadiene with maleic anhydride) was converted by heating with phosphorus pentoxide to o-dichlorobenzene (VI; yield 50%), identified by its constants and the melting point of its sulfamide.



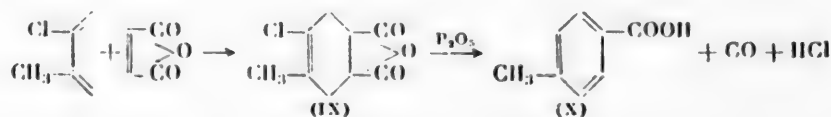
The diene synthesis with chloroprene and methylmaleic anhydride has not been yet described. This reaction succeeded under the conditions we set up for the experiment (heating of the reactants in propionic acid for 17 hr); the basic product was 4-chloro-2-methyl-1,2,3,6-tetrahydrophthalic acid (VII), i.e., the "meta" adduct (yield 51%). The structure of this adduct (VII) is proved by its conversion upon heating with phosphorus pentoxide to m-chlorotoluene\* (VIII, yield 47.5%), identified by the melting point of its sulfamide and its oxidation to m-chlorobenzoic acid (p-chlorobenzoic acid could not be detected).



The study of the infrared absorption spectrum of the chlorotoluene thus obtained showed that it contained traces of p-chlorotoluene (beside the absorption bands in the region of 680 and 774 cm<sup>-1</sup>, characteristic for the meta isomer, there were also absorption bands in the region of 808 and 732 cm<sup>-1</sup>, characteristic for the para isomer); however, the p-chlorotoluene content was so insignificant that it could not be detected by chemical means.

The condensation of chloroprene with various dienophiles of unsymmetric structure is described in the literature [2]; in all cases the reaction products were the so-called "para" adducts, i.e., adducts with substituents in 1,4-positions. The preferential formation of the "meta" adduct during the reaction of chloroprene with methylmaleic anhydride can be probably explained by the fact that we prepared it by heating in propionic acid, while the "para" adducts of chloroprene described previously have been obtained by heating in non-polar solvents (benzene, toluene).

A further study of the behavior of halogen-substituted tetrahydrophthalic acids toward phosphorus pentoxide gave unexpected results: The chloro-substituted methyltetrahydrophthalic anhydride with the same position of chlorine atom in the ring, but with a different position of the methyl group than in the adduct (VII), viz., 5-chloro-4-methyl-1,2,3,6-tetrahydrophthalic anhydride (IX, adduct of methylchloroprene with maleic anhydride) gave, instead of the expected o-chlorotoluene, p-toluic acid, identified by the melting point of its p-bromophenacyl ester.



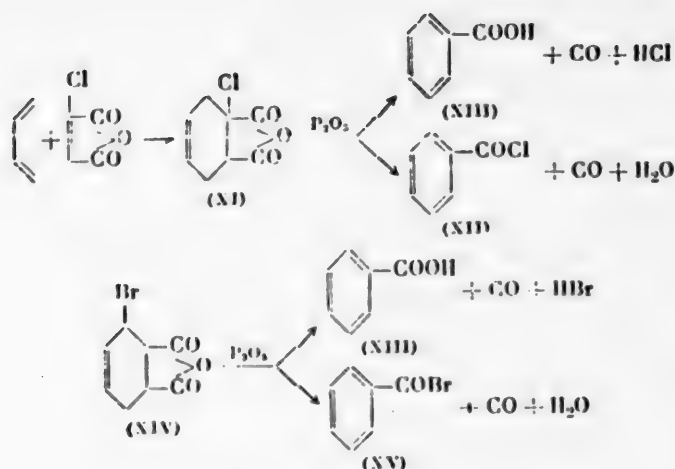
Therefore, in this reaction one molecule of hydrogen chloride and one molecule of carbon monoxide were split off.

Further, it appeared that such an anomalous course of the reaction is also displayed by other halogen-substituted tetrahydrophthalic acids. Thus, to give an example, 2-chloro-1,2,3,6-tetrahydrophthalic anhydride (XI, adduct of divinyl with chloromaleic anhydride) and 3-bromo-1,2,3,6-tetrahydrophthalic anhydride (XIV, obtained by bromination of tetrahydrophthalic anhydride with N-bromosuccinimide)\*\* are converted upon reaction with phosphorus pentoxide to benzoic acid (XIII); however, in these two cases (in distinction to the preceding) one could isolate from the reaction products also the corresponding haloanhydrides of benzoic acid (XII, XV). With the help of specially designed experiments, it was proved that the formation of the haloanhydrides of benzoic acid is not due to the reaction of benzoic acid with hydrogen halides in the presence of phosphorus pentoxide.

\* It has been shown that even upon prolonged heating (under reflux), phosphorus pentoxide does not provoke isomerization of either m- or p-chlorotoluene.

\*\* 3-Substituted halogen derivatives of tetrahydrophthalic anhydride cannot be obtained by reaction of 1-halo-1,3-butadienes with maleic anhydride [3].





It follows that halogen-substituted tetrahydrophthalic acids and their anhydrides do not undergo aromatization (under the influence of phosphorus pentoxide) according to the normal scheme (i.e., with the formation of arylhalogenides) if they easily split off a hydrogen halide.

#### EXPERIMENTAL

**4-Chloro-1,2,3,6-tetrahydrophthalic anhydride (I).** Chloroprene (44 g) and maleic anhydride (49 g) were cautiously heated to 50° in the presence of hydroquinone (0.1 g) in a flask fitted with a reflux condenser; after the spontaneous boiling had subsided, the mixture was allowed to stand overnight. The anhydride (I) which separated out [yield 75 g (76.5%), not described in the literature] melted at 60° after recrystallization from petroleum ether.

Found %: C 51.22, 51.31; H 3.65, 3.68; Cl 19.13, 19.25.  $C_8H_7O_3Cl$ . Calculated %: C 51.47; H 3.75; Cl 19.03.

Heating of the anhydride (I) with water gave 4-chloro-1,2,3,6-tetrahydrophthalic acid, m. p. 172°, which is consistent with the published data [4].

**4-Bromo-1,2,3,6-tetrahydrophthalic acid (III).** Bromoprene (20 g, b. p. 75-77°,  $n_D^{20}$  1.4991, obtained by the action of potassium hydroxide on 3,4-dibromo-1-butene [5]), and maleic anhydride (12 g) were slightly heated on a water bath in the presence of hydroquinone (0.1 g); after the maleic anhydride had dissolved, the mixture was allowed to stand overnight. It was then heated for 2 hr on a boiling water bath, and the unreacted bromoprene was distilled off under reduced pressure (200-220 mm). The residue thus obtained was dissolved in a large volume of benzene, the benzene solution extracted with 2N sodium hydroxide solution, and the aqueous extract neutralized with concentrated hydrochloric acid. Concentration of the solution led to the separation of the acid (III) melting at 175° (reported in the literature [6]; m. p. 176.5°).

**4,5-Dichloro-1,2,3,6-tetrahydrophthalic acid (V).** 2,3-Dichlorobutadiene (15 g, b. p. 40-42° (80 mm),  $n_D^{20}$  1.5010, prepared from vinylacetylene [7]) and maleic anhydride (12 g) in dry benzene (200 ml) were heated in an autoclave (100°, 7 hr) in the presence of hydroquinone (0.1 g). The crystalline mass formed after cooling the mixture and distilling off the solvent was boiled with 10 times its weight of water. 4,5-Dichloro-1,2,3,6-tetrahydrophthalic acid (V) which separated out [yield 20 g (74%)] melted after recrystallization from aqueous alcohol at 230° (reported m. p. 228° [7]).

**4-Chloro-2-methyl-1,2,3,6-tetrahydrophthalic acid (VII).** Chloroprene (12 g) and methylmaleic anhydride (30.4 g, twofold excess) in propionic acid (50 ml) were refluxed for 17 hr in the presence of hydroquinone and picric acid (0.1 g of each). The propionic acid and excess of methylmaleic anhydride were distilled off in vacuum. The adduct boiling at 160-165° (10 mm) was then distilled, dissolved in 2N sodium hydroxide, boiled with activated charcoal, and treated with concentrated hydrochloric acid to precipitate 4-chloro-2-methyl-1,2,3,6-tetrahydrophthalic acid [VII, yield, 15 g (51%) m. p. 157°, not described in the literature].

Found %: C 49.69, 49.42; H 5.12, 5.18; Cl 15.65, 15.76.  $C_9H_{11}O_4Cl$ . Calculated %: C 49.45; H 5.07; Cl 16.23.

Data concerning the reaction of chloroprene with methylmaleic anhydride under different conditions are given in the following table.

Reaction of Chloroprene with Methylmaleic Anhydride

Proportions of the re-actants	Solvent	Temperature	Reaction time (hr)	Yield of the adduct (%)
1:1	Without solvent	69-70°	3	—
1:1	Without solvent	100	6	—
1:1	Without solvent	50 (in autoclave)	12	—
1:1	Without solvent	80 (in autoclave)	15	15.5
1:3	Propionic acid	Boiling point of the mixture	17	43.5
1:2	Propionic acid	Boiling point of the mixture	17	51.0

5-Chloro-4-methyl-1,2,3,6-tetrahydrophthalic anhydride (IX). Methylchloroprene (28 g, m. p. 92-95° at 751 mm,  $n_D^{20}$  1.4680, prepared from dimethylethynylcarbinol [8]), and maleic anhydride (27 g) in dry toluene (50 ml) were heated for 7 hr (in the presence of hydroquinone). The reaction mixture was cooled to room temperature, diluted with a large volume of petroleum ether, and cooled to 0°. The crystalline adduct (IX) which separated out (50 g, 90%) was distilled in vacuum [b. p. 176-178° (5 mm)] and recrystallized from petroleum ether; m. p. 78°. Reported [5]: m. p. 79-80°, b. p. 196° (15 mm).

1-Chloro-1,2,3,6-tetrahydrophthalic anhydride (XI). Chloromaleic anhydride (32 g) (obtained by a series of reactions from tartaric acid [10]), divinyl (20 ml), and dry benzene (100 ml) together with small amounts of hydroquinone (0.2 g) and picric acid (0.5 g) were left to stand at room temperature in a stoppered flask for 7 days. The residue obtained after evaporation of benzene was distilled in vacuum, giving 20 g (38%) of 4-chloro-1,2,3,6-tetrahydrophthalic anhydride (XI), b. p. 105-110° (2 mm). Reported b. p. [11]: 115° (5 mm).

3-Bromo-1,2,3,6-tetrahydrophthalic anhydride (XIV). A mixture of  $\Delta^4$ -tetrahydrophthalic anhydride (15.2 g, m. p. 161-163°, obtained from divinyl and maleic anhydride [12]), and *N*-bromosuccinimide (18.3 g, m. p. 175°) in dry chloroform (75 ml) was heated to boiling. The reaction was considered to be completed when a sample of the mixture gave a negative test for active bromine with a solution of potassium iodide. The succinimide formed was filtered off, the chloroform removed by distillation in vacuum, and the thick mass thus obtained was washed with a large amount of petroleum ether (to remove the starting anhydride). 3-Bromo-2,3,6-tetrahydrophthalic anhydride (XIV) isolated by this procedure was made to react with phosphorus pentoxide without further purification. It was not possible to purify this anhydride by recrystallization or distillation in vacuum, as it split off hydrogen bromide even upon slight heating.

#### Reaction of the Prepared Anhydrides and Acids with Phosphorus Pentoxide

4-Chloro-1,2,3,6-tetrahydrophthalic anhydride (I) (20 g) and phosphorus pentoxide (15.2 g) were gradually heated on a metal bath to 160-200° (the reaction was accompanied by strong evolution of carbon monoxide); the chlorobenzene (II) thus formed was immediately distilled off, submitted to steam-distillation, dried over calcium chloride, and redistilled. Yield, 5.5 g (45%).

B. p. 130-131° (760 mm),  $n_D^{20}$  1.5239,  $d_4^{20}$  1.1060; sulfonamide derivative m. p. 144-145° (from aqueous alcohol), gives no m. p. depression when mixed with the sulfonamide of an authentic sample of chlorobenzene. Reported in the literature [13]: b. p. 132-133° (corrected),  $n_D^{20}$  1.5248,  $d_4^{20}$  1.1066.

4-Bromo-1,2,3,6-tetrahydrophthalic acid (III) (6.5 g) under analogous conditions (with 7.4 g of phosphorus pentoxide) was converted to bromobenzene (IV) [yield, 1.7 g (42.5%)], the sulfonamide derivative of which melted at 159-160° (from diluted alcohol). Reported m. p. 161.5° [14].

4,5-Dichloro-1,2,3,6-tetrahydrophthalic acid (V) (18 g), when heated with phosphorus pentoxide (21 g), gave *o*-dichlorobenzene (VI) [yield, 5.9 g (50%)].

B. p. 180.5° (746 mm),  $n_D^{20}$  1.5506,  $d_4^{20}$  1.3042; sulfonamide derivative m. p. 133-134°. Reported in the literature: b. p. 180.3° (750 mm),  $n_D^{20}$  1.5513,  $d_4^{20}$  1.3050 [15]; sulfonamide m. p. 134-135° [14].

4-Chloro-2-methyl-1,2,3,6-tetrahydrophthalic acid (VII) (11 g), upon heating (200-250°) with phosphorus pentoxide (14.2 g), was converted to m-chlorotoluene (VIII) [yield, 3 g (47.5%)].

B. p. 161.5° (750 mm),  $n_D^{20}$  1.5196,  $d_4^{20}$  1.0715. Reported [16] for m-chlorotoluene: b. p. 162°,  $n_D^{20}$  1.5214,  $d_4^{20}$  1.0722; for p-chlorotoluene: b. p. 162°,  $n_D^{20}$  1.5199,  $d_4^{20}$  1.0697.

The sulfonamide derivative of VIII melted after a single recrystallization from alcohol at 182°; this is in agreement with the reported m. p. for the sulfonamide of m-chlorotoluene [14]; the sulfonamide of p-chlorotoluene has m. p. 142-143° [14]. The sulfonamide of VIII did not depress the m. p. of the sulfonamide of an authentic sample of m-chlorotoluene. The oxidation product of VIII with manganese dioxide in sulfuric acid [17] yielded only one acid with m. p. 159-160°, which corresponds to the reported value for m-chlorobenzoic acid [17] (p-chlorobenzoic acid melts at 243° [17]).

5-Chloro-4-methyl-1,2,3,6-tetrahydrophthalic anhydride (IX) (16 g) and phosphorus pentoxide (11.5 g) were heated on a metal bath at 180-300° in a flask with a reflux condenser until evolution of gaseous reaction products ceased. The reaction mixture was extracted with ether; the residue obtained after evaporation of the solvent was dissolved in 2N alkali and precipitated with hydrochloric acid. The substance which separated out appeared to be p-toluic acid (X) [yield, 3.5 g (42%)]; it was purified by sublimation, m. p. 175°; m. p. of its p-bromophenacyl ester, 151.5°. Reported m. p. of p-toluic acid: 176-178° [18]; of the p-bromophenacyl ester of p-toluic acid: 153° [19]. A strong evolution of hydrogen chloride was observed during the reaction. Analysis of the gases produced showed there was also evolution of carbon monoxide (70%), and, to a certain degree, decarboxylation (15%). It was not possible to isolate o-chlorotoluene from the reaction product.

2-Chloro-1,2,3,6-tetrahydrophthalic anhydride (XI) (35 g) and phosphorus pentoxide (35.5 g) were heated for 40 min. The reaction products were distilled in vacuum and then redistilled. Two substances were isolated: benzoyl chloride (XII) [yield, 3.5 g (14%), b. p. 89-190° at 745 mm,  $n_D^{20}$  1.5537; benzamide derivative m. p. 130°], and benzoic acid (XIII) [yield, 5.4 g (20%) m. p. 121°].

3-Bromo-1,2,3,6-tetrahydrophthalic anhydride (XVI) (43 g) was gradually heated with phosphorus pentoxide (26.5 g) under the conditions described for 5-chloro-4-methyl-1,2,3,6-tetrahydrophthalic anhydride (IX). The reaction products gave benzoyl bromide (XV) (2 g, identified by its conversion to benzoic acid) and benzoic acid (XIII) (4 g, m. p. 122°).

## SUMMARY

1. It has been shown for the first time that halogen-substituted tetrahydrophthalic acids and their anhydrides (adducts of halogen-substituted dienes with maleic and methylmaleic anhydrides) are aromatized under the action of phosphorus pentoxide to aryl halides, the reaction proceeding with elimination of two molecules of carbon monoxide and water. Thus, the adducts of chloroprene, bromoprene and 2,3-dichloro-1,3-butadiene with maleic and methylmaleic anhydrides gave chlorobenzene, bromobenzene, o-dichlorobenzene, and m-chlorotoluene, respectively.

2. Halogen-substituted tetrahydrophthalic acids and their anhydrides, if they easily lose hydrogen halides, undergo under the action of phosphorus pentoxide a reaction of another type: They eliminate one molecule of carbon monoxide and one of the hydrogen halide, with the formation of an aryl carboxylic acid, together with the haloanhydride of the same acid.

3. The diene synthesis (by heating in propionic acid) of chloroprene with an asymmetrical dienophile, viz., methylmaleic anhydride, has been carried out; the reaction product was a so-called "meta" adduct, viz., 4-chloro-2-methyl-1,2,3,6-tetrahydrophthalic acid.

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## INVESTIGATIONS IN THE FIELD OF ALKANESULFONIC ACIDS

### XXIII. SYNTHESIS AND PROPERTIES OF SOME ESTERS OF METHANESULFONIC ACID

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The esters of alkanesulfonic acids possess many valuable properties. Thus, the methyl esters of the higher alkanesulfonic acids have been used as plasticizers for vinyl resins, some esters are solvents for film-forming substances, and many esters are known as good plasticizers and softeners for polyvinyl chlorides, chloro-rubbers, and nitrocellulose [1]. Di-(methanesulfonate)-1,4-butanediol, known under the name of "Myleran", has found a clinical application in the treatment of myelitic leucosis [2]. The esters of alkanesulfonic acids with ethylene chlorohydrin also possess an anticarcinogenic activity [3].

The aim of the present work was to synthesize some esters of methanesulfonic acid already described in the literature, but unsufficiently characterized, and to prepare new esters.

We obtained the di-methanesulfonate of ethylene glycol (I), the di-methanesulfonate of  $\alpha, \gamma$ -butylene glycol (III), the tri-methanesulfonate of ethylene chlorohydrin (IV), the di-methanesulfonate of glycerol  $\alpha$ -chlorohydrin (V); I, III, and IV were already described in the literature [3, 4], while II and V are now prepared for the first time.

The reaction was carried out by mixing methanesulfonic acid chloride with the corresponding alcohol in pyridine with cooling, followed by precipitation of the ester by acidification. The esters II-V have been obtained in good yields, I in low yield.

#### EXPERIMENTAL

Synthesis of esters of methanesulfonic acid with polyalcohols and chlorohydrins. Freshly distilled ethylene glycol (b. p. 85° at 5 mm),  $\alpha, \gamma$ -butylene glycol (b. p. 205.5°), ethylene chlorohydrin (b. p. 128°), chemically pure glycerol, and glycerol  $\alpha$ -chlorohydrin (b. p. 119° at 15 mm) were used in the reactions.

The calculated amount of the corresponding alcohol was dissolved in freshly distilled pyridine with cooling to 0°. The solution was then treated, dropwise and while stirring, with methanesulfonyl chloride. After a while, pyridine hydrochloride precipitated out. The reaction mixture was allowed to stand at room temperature for 24 hr. The ester was then precipitated from the pyridine solution by addition of cooled diluted sulfuric acid (1:3); it separated out as an oily layer at the bottom of the flask. To complete the separation of the ester, the reaction mixture was kept for 16 hr in the cold. The ester was then extracted thrice with chloroform; the combined extracts were washed with water and dried over anhydrous sodium sulfate. The solvent was distilled off, and the residue was distilled in vacuum in the case of liquid esters, or crystallized from alcohol in the case of solid esters. Experiments were also carried out without extraction with chloroform, but the yields were much lower.

The yields and properties of the esters synthesized in these experiments are given in the following table.



# Esters of Methanesulfonic Acids

No.	Name and formula of the ester	Starting material (in g)		Amount of pyridine (in ml)	Yield of the ester (in %)	M. p.	% S	
		alcohol	CH <sub>3</sub> SO <sub>2</sub> Cl				found	calcd.
1	Glycol di-methanesulfonate C <sub>4</sub> H <sub>10</sub> O <sub>6</sub> S <sub>2</sub>	2.0	6.5	5	21.4	44-45°	28.98	29.36
2	α, γ-Butylene glycol di-methanesulfonate C <sub>6</sub> H <sub>14</sub> O <sub>6</sub> S <sub>2</sub>	2.24	5.7	15	45.0	40-41°	25.84	26.06
3	Glycerol tri-methanesulfonate C <sub>6</sub> H <sub>14</sub> O <sub>9</sub> S <sub>3</sub>	3.6	11.2	15	78.8	77-78°	29.32	29.44
4	Ethylene chlorohydrin methanesulfonate* C <sub>2</sub> H <sub>5</sub> O <sub>3</sub> SCl	4.2	6.0	10	57.8	-	19.81 Cl 22.61	20.18 22.40
5	Glycerol α-monochlorohydrin di-methanesulfonate C <sub>5</sub> H <sub>11</sub> O <sub>6</sub> S <sub>2</sub> Cl	4.3	8.0	15	69.4	67-68°	23.85 Cl 13.50	24.05 13.30

\*B.p. 126° (10 mm), n<sub>D</sub><sup>20</sup> 1.4590, d<sub>4</sub><sup>20</sup> 1.3837, MR<sub>D</sub> 31.32; calc. 31.17.

The esters I-III and V appear as crystalline substances with a slight pink coloration; they are odorless (with the exception of III, which has a fine pleasant odor); they do not dissolve in water and ether, but are readily soluble in chloroform, acetone, and upon warming, in alcohol. The ester IV is a colorless mobile liquid, odorless and bitter.

## SUMMARY

The methanesulfonates of ethylene glycol, α, γ-butylene glycol, ethylene chlorohydrin, glycerol and glycerol α-monochlorohydrin have been synthesized and characterized, the esters of α, γ-butylene glycol and glycerol α-monochlorohydrin being obtained for the first time.

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# SYNTHESIS AND PROPERTIES OF BRANCHED ACIDS.

## SERIES $C_nH_{2n} + 1COOH$ , COMPOSITION $C_{12}-C_{20}$ . II.

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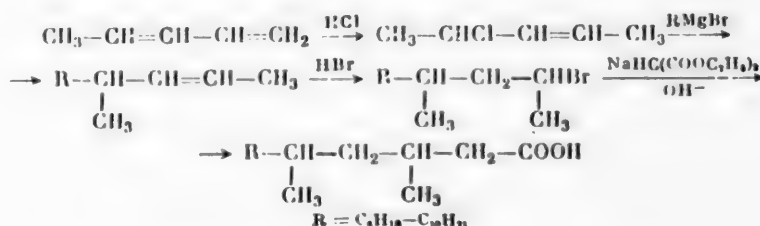
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We had previously accomplished the synthesis of acids with the composition  $C_{12}-C_{16}$  and of the type  $R-CH(CH_3)-CH_2-CH(CH_3)COOH$  by the organomagnesium method [1]. In the present work we obtained a series of acids by the malonic acid synthesis according to the scheme:



Both studies were undertaken to learn about the physical properties of branched acids, and the surface-active and detergent properties of their sodium salt solutions. Up to now these properties have remained unexplored, while there are data on the improved solubility of magnesium and sodium salts of branched acids as compared to those of normal acids with similar mol. wt. [2]. The good solubility of branched acid salts can be very useful in their application to formulating detergents or manufacturing soaps.

With the exception of the last stage, all synthesis stages as pictured in the scheme above and also the properties of intermediate products (2-alkyl pentenes-3 and 2-alkyl-4-bromopentane) have been described in a previous communication [1]. The malonic synthesis of acids was accomplished in the usual way: From 2-alkyl-4-bromopentanes and sodium ethyl malonate were prepared the corresponding ethyl esters of alkyl malonic acids, with a 30-60% yield. The properties of these esters are given in Table 1. Exaltation was observed when molecular refraction of malonic esters was computed from the magnitudes of bond increments, as proposed by Vogel et al. [3]; for esters of type  $RCH(CH_3)CH_2CH(CH_3)CH(COOC_2H_5)_2$  the average exaltation value was +0.61. Table 1 also gives ethyl esters of alkyl-(dialkyl)malonic acids of another type, which we had investigated during the synthesis of  $C_{18}$  and  $C_{20}$  acids. When malonic esters were boiled with a 33% solution of NaOH or KOH and the alkyl malonic acids vacuum distilled, monobasic acids were obtained (92-96% yield), the structures and properties of which are given in Table 2. These acids are colorless, viscous liquids, with no odor. They are also characterized by molecular refraction exaltation, the average value of which is +0.37 for acids with the structure

TABLE 1

Ethyl esters of alkylmalonic acids	Composition	Boiling point (pressure in mm)	$d_4^{20}$	$n_D^{20}$	MRD	
					found	calculated
$C_9H_{13}-CH-CH_2-CH-CH(COOC_2H_5)_2$ $\begin{array}{c}   \\ CH_3 \end{array}$ $\begin{array}{c}   \\ CH_3 \end{array}$	$C_{18}H_{34}O_4$	140—142°(1)	0.9368	1.4407	88.59	89.22
$C_7H_{15}-CH-CH_2-CH-CH(COOC_2H_5)_2$ $\begin{array}{c}   \\ CH_3 \end{array}$ $\begin{array}{c}   \\ CH_3 \end{array}$	$C_{16}H_{30}O_4$	120—122 (0.5)	0.9328	1.4423	93.21	93.87
$C_9H_{17}-CH-CH_2-CH-CH(COOC_2H_5)_2$ $\begin{array}{c}   \\ CH_3 \end{array}$ $\begin{array}{c}   \\ CH_3 \end{array}$	$C_{20}H_{38}O_4$	166—167 (1)	0.9288	1.4435	97.92	98.52
$C_9H_{19}-CH-CH_2-CH-CH(COOC_2H_5)_2$ $\begin{array}{c}   \\ CH_3 \end{array}$ $\begin{array}{c}   \\ CH_3 \end{array}$	$C_{21}H_{40}O_4$	152—153 (0.5)	0.9241	1.4445	102.57	103.17
$C_{10}H_{21}-CH-CH_2-CH-CH(COOC_2H_5)_2$ $\begin{array}{c}   \\ CH_3 \end{array}$ $\begin{array}{c}   \\ CH_3 \end{array}$	$C_{22}H_{42}O_4$	161—162 (0.5)	0.9206	1.4453	107.24	107.82
$C_4H_9-CH-CH-CH_2-CH(COOC_2H_5)_2$ $\begin{array}{c}   \\ CH_3 \end{array}$ $\begin{array}{c}   \\ CH_3 \end{array}$ $\begin{array}{c}   \\ CH_3 \end{array}$	$C_{15}H_{28}O_4$	126—127 (3)	0.9487	1.4340	74.76	75.28
$(C_4H_9-CH-CH_2)_2C(COOC_2H_5)_2$ $\begin{array}{c}   \\ C_2H_5 \end{array}$	$C_{23}H_{44}O_4$	148—150 (2)	0.9292	1.4492	111.05	112.46
$C_{10}H_{21}(C_4H_9-CH-CH_2)C(COOC_2H_5)_2$ $\begin{array}{c}   \\ C_4H_9 \end{array}$ $\begin{array}{c}   \\ C_4H_9 \end{array}$	$C_{25}H_{48}O_4$	178—182 (0.5)	0.9154	1.4488	120.79	121.76

TABLE 2

Acids	Composition	Molecu- lar weight*	B.p. (mm Hg)	$d_{20}^{20}$	$n_D^{20}$	MR D		Found %		Calculated %	
						found	calcd.	C	H	C	H
$C_6H_{13}-CH-CH_2-CH-CH_2COOH$ $\begin{array}{c} CH_3 \\   \\ CH_3 \end{array}$	$C_{13}H_{26}O_2$	216.7	120-121 (1.5)	0.8920	1.4436	63.78	64.05	72.54, 72.66	11.70, 11.90	72.84	12.32
$C_7H_{15}-CH-CH_2-CH-CH_2COOH$ $\begin{array}{c} CH_3 \\   \\ CH_3 \end{array}$	$C_{14}H_{28}O_2$	245.4	122-124 (0.5)	0.8910	1.4458	68.32	68.70	73.65, 73.40	12.05, 12.27	73.66	12.36
$C_8H_{17}-CH-CH_2-CH-CH_2COOH$ $\begin{array}{c} CH_3 \\   \\ CH_3 \end{array}$	$C_{15}H_{30}O_2$	230.4	172-174 (2)	0.8893	1.4475	72.90	73.34	74.02, 74.26	12.33, 12.54	74.32	12.48
$C_9H_{19}-CH-CH_2-CH-CH_2COOH$ $\begin{array}{c} CH_3 \\   \\ CH_3 \end{array}$	$C_{16}H_{32}O_2$	258.3	147-149 (0.5)	0.8859	1.4491	77.63	77.99	74.86, 74.71	12.48, 12.40	74.94	12.58
$C_{10}H_{21}-CH-CH_2-CH-CH_2COOH$ $\begin{array}{c} CH_3 \\   \\ CH_3 \end{array}$	$C_{17}H_{34}O_2$	271.7	166-168 (1)	0.8834	1.4498	82.24	82.64	75.17, 75.02	12.45, 12.51	75.49	12.67
$(C_4H_9-CH-CH_2)_2CHCOOH$ $\begin{array}{c} CH_3 \\   \\ CH_3 \end{array}$	$C_{18}H_{36}O_2$	286.4	148-150 (1.5)	0.8922	1.4486	86.59	87.35	76.02, 76.02	12.61, 12.60	75.99	12.76
$C_{10}H_{21}(C_4H_9CH-CH_2)-CHCOOH$ $\begin{array}{c} C_2H_5 \\   \\ C_2H_5 \end{array}$	$C_{20}H_{40}O_2$	312	164-165 (0.5)	0.8767	1.4518	96.10	96.65	76.82, 77.03	12.75, 12.72	76.88	12.90

\* Calculated from acid number.

TABLE 3

Acids	Viscosity (in centistokes)				Congeal- ing point
	20°	50°	75°	100°	
$\begin{array}{c} \text{R}-\text{CH}-\text{CH}_2-\text{CH}-\text{COOH} \\   \qquad \qquad   \\ \text{CH}_3 \qquad \text{CH}_3 \end{array} \text{ Type I}$					
R=C <sub>6</sub> H <sub>13</sub> —	37.17	10.59	5.18	—	—62°
R=C <sub>7</sub> H <sub>15</sub> —	40.48	11.85	5.78	3.57	—59
R=C <sub>8</sub> H <sub>17</sub> —	44.82	12.91	6.24	3.59	—59
R=C <sub>9</sub> H <sub>19</sub> —	52.58	15.19	7.41	4.39	—58
R=C <sub>10</sub> H <sub>21</sub> —	61.44	17.33	8.20	4.77	—52
$\begin{array}{c} \text{C}_4\text{H}_9-\text{CH}-\text{CH}_2-\text{CH}-\text{CH}_2-\text{CH}-\text{COOH} \\   \qquad \qquad   \qquad \qquad   \\ \text{C}_2\text{H}_5 \qquad \text{CH}_3 \qquad \text{CH}_3 \end{array}$	60.86	14.12	6.31	3.65	—
$\begin{array}{c} \text{C}_6\text{H}_{13}-\text{CH}-\text{CH}-\text{CH}_2-\text{CH}-\text{COOH} \\   \qquad   \qquad \qquad   \\ \text{CH}_3 \qquad \text{CH}_3 \qquad \text{CH}_3 \end{array}$	67.65	16.38	7.52	4.24	—
$\begin{array}{c} \text{R}-\text{CH}-\text{CH}_2-\text{CH}-\text{CH}_2\text{COOH} \\   \qquad \qquad   \\ \text{CH}_3 \qquad \text{CH}_3 \end{array} \text{ Type II}$					
R=C <sub>6</sub> H <sub>13</sub> —	39.05	11.57	5.73	—	—62
R=C <sub>7</sub> H <sub>15</sub> —	43.90	12.99	6.69	—	—59
R=C <sub>8</sub> H <sub>17</sub> —	51.16	14.93	7.38	—	—58
R=C <sub>9</sub> H <sub>19</sub> —	60.01	17.06	8.16	—	—58
R=C <sub>10</sub> H <sub>21</sub> —	70.24	19.19	9.01	—	—52
$\begin{array}{c} (\text{C}_4\text{H}_9-\text{CH}-\text{CH}_2)_2\text{CHCOOH} \\   \\ \text{C}_2\text{H}_5 \end{array}$	146.79	28.64	11.37	5.73	—50
$\begin{array}{c} \text{C}_{10}\text{H}_{21}(\text{C}_4\text{H}_9-\text{CH}-\text{CH}_2)_2\text{CHCOOH} \\   \\ \text{C}_2\text{H}_5 \end{array}$	101.22	24.75	10.77	5.71	—28

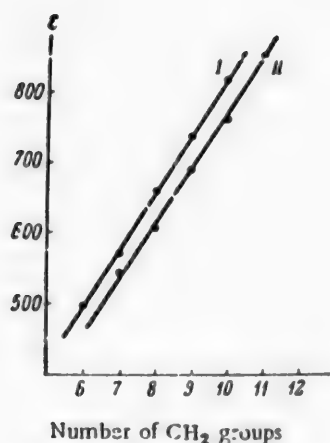
R-CH(CH<sub>3</sub>)-CH<sub>2</sub>-CH(CH<sub>3</sub>)-CH<sub>2</sub>COOH (type II). For acids of type I, structure R-CH(CH<sub>3</sub>)-CH<sub>2</sub>-CH(CH<sub>3</sub>)-COOH, we could detect no regularity in the difference between the found and the calculated M<sub>RD</sub> values [1]. Table 3 gives the congealing point and the kinematic viscosity of the acids, the synthesis of which had previously been described and is being reported in the current communication.

All acids, with the exception of those having the n-decyl radical in their structure, congealed to a transparent "glass." When the ones containing the n-decyl radical were cooled, a crystalline phase appeared. The congealing points were determined by standard means, from the rate of meniscus shift when the acid is placed in a test tube of 13 mm internal diameter of a 45° angle off the vertical [4]. The viscosities of acids of types I and II, with the same molecular weights (provided R is a normal alkyl radical), are very close. Compared to the viscosity of normal acids at 75° (lauric acid 4.50 centistokes, tetradecanoic 5.96, and palmitic 8.38 [5]), that of the ones synthesized by us was somewhat higher for C<sub>12</sub> (5.18) and C<sub>14</sub> (6.24; 6.69; 6.31; 7.52) and somewhat lower for C<sub>16</sub> (8.16). Specific gravities and refractive indices measured at 75° were, in the case of branched hexadecanoic acids:



and proved to be very close to the corresponding values characterizing palmitic acid ( $d_4^{75}$  0.8446,  $n_D^{75}$  1.4288 [5]). Infrared spectra were taken of acids I and II. It was established that the intensity of the band 2930 cm<sup>-1</sup>





( $\epsilon$ ), which corresponds to the asymmetric valence vibrations in group  $\text{CH}_2$ , is linearly dependent on the number of  $\text{CH}_2$  groups in the acid molecule. The relationship is expressed by two parallel lines. For acids of type II, as a result of lesser intensity of the  $\text{CH}_2$  group in  $\alpha$  position to the carbonyl group, the dependency line is below that characterizing acids of type I (see figure). The spectra of acids were obtained on an infrared spectrometer IKS-12 [IRS-12] with a LiF prism in the  $2800\text{--}3100\text{ cm}^{-1}$  region. Samples were tested in a 0.1%  $\text{CCl}_4$  solution.\*

#### EXPERIMENTAL

We shall describe the synthesis of branched acids on only two examples — through the ethyl esters of monoalkyl- and dialkylmalonic acids. The rest of the acids, the structures and properties of which are given in Table 2, were prepared analogously.

3,5-Dimethyltetradecanoic acid. a) To 250 ml anhydrous alcohol was added gradually 14.3 g (0.62 gram atom) sodium, 100 g (0.6 mole) malonic ester, and 170 g (0.6 mole) 4-methyl-2-bromotridecane. The mixture was boiled for 10.5 hours, after which sodium bromide was separated from it and some alcohol distilled off. The residue was treated with water, dried, and vacuum distilled. Ethyl ester of (1,3-dimethyldodecyl)malonic acid was obtained (35.4%, or 80.4 g). b) The ester thus obtained, 71 g (0.2 mole), was digested for 6–12 hr with an excess of 33% NaOH, after which the unreacted malonic ester was extracted with ether and the alkaline mass treated with HCl. Obtained was 47 g of 3,5-dimethyltetradecanoic acid in 92% yield.

Di-(2-ethylhexyl)acetic acid. a) To 900 ml alcohol was added 39 g (1.7 gram atom) sodium, 270 g (1.7 mole) malonic ester, and 318 g (1.65 mole) 2-ethylhexyl bromide. The reaction mass was boiled for 9.5 hr, after which it was worked up in a manner analogous to that described above to give 285 g (63%) of the ethyl ester of 2-ethylhexylmalonic acid and 20 g of the di-(2-ethylhexyl)malonate. b) From 136 g (0.5 mole) ethyl ester of 2-ethylhexylmalonic acid, 136 g (0.7 mole) 2-ethylhexyl bromide, and 14 g (0.6 gram atom) sodium in 350 ml alcohol was obtained, after boiling for 9 hr, 73 g ethyl ester of di-(2-ethylhexyl)malonic acid, or 38% yield. More than half of the initial ester was recovered from the reaction mixture. c) Di-(2-ethylhexyl)-acetic acid was obtained in 53% yield, or 20 g, when 75 g (0.2 mole) of ester obtained was boiled for 8 hr with a solution of 66 g (1.18 mole) KOH in 70 ml water and the alkaline mass treated with HCl.

#### SUMMARY

1. A number of acids with the composition  $\text{C}_{13}\text{--C}_{20}$  and two branches to the main hydrocarbon chain were prepared by the malonic synthesis.
2. Congealing points and kinematic viscosities were determined for branched acids with the composition  $\text{C}_{12}\text{--C}_{20}$ .

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\* For the Infrared spectra we are indebted to R. A. Grinberg.

## PHYSICAL PROPERTIES OF 1,4-DIALKYL CYCLOHEXANES

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We had prepared and characterized 1,4-dialkylbenzenes [1] during former studies of surface active properties of sodium dialkylbenzenesulfonates:



where R is a normal alkyl radical  $\text{C}_4\text{-C}_9$ .










In the present work we accomplished the hydrogenation of p-dialkylbenzenes and learned about some physical properties of 1,4-dialkylcyclohexanes prepared for the first time. The hydrogenation was carried out in a rotary autoclave at 210-230° and initial pressure of 110-130 atm over Raney nickel. For each experiment 8-10 g of a pure sample was used. The dialkylcyclohexanes were separated from the unhydrogenated dialkylbenzenes chromatographically in a column filled with silica gel (150-200 mesh). After purification in the column, dihexyl-, diheptyl-, dioctyl-, and dinonylcyclohexanes were recrystallized from alcohol at 0-2°. Their capillary melting points were determined, the capillary being placed in a metal block provided with an electric heating device. The melting points of dihexyl- and diheptylcyclohexanes were determined in a special chamber where the temperature was maintained at 0-2°.

Table 1 gives the properties of 1,4-dialkylcyclohexanes. In order to compare these properties with those of monoalkylcyclohexanes of similar molecular weights, we included in the table octyl- and dodecylcyclohexanes prepared by us. The synthesis of the latter compounds was accomplished by hydrogenation of octyl- and dodecylbenzenes, which in turn were obtained by the Grignard-Wurtz reaction from bromobenzene, octyl bromide, and dodecyl bromide. The physical constants of 1,4-dialkylcyclohexanes (with normal alkyl radicals) are very close to those of monoalkylcyclohexanes of similar molecular weights, and the melting points of dodecyl-, tetradecyl-, hexadecyl-, and octadecylcyclohexanes are respectively 12, 25, 32, and 40° [2, 3]. There is a straight line correlation between the magnitudes of melting points,  $d_4^{20}$ ,  $n_D^{20}$  and the number of carbon atoms in the alkyl radical of 1,4-dialkylcyclohexanes; this is graphically illustrated in Fig. 1. The average value for the exaltation of molecular refraction ( $\Delta \text{MR}_D$ ) for compounds (I-VI) (Table 1) is +0.10. The molecular refractions were calculated from bond refractions, as proposed by Vogel et al. [4].

Kinematic viscosity at -40, -20, 0, 20, 50, and 75° was determined for di- and monoalkylcyclohexanes with the Ostwald viscosimeter. At -40 and -20° the accuracy of the temperature measurements was  $\pm 0.3^\circ$ , at 0, 20, 50, and 75°  $\pm 0.1$ . The viscosity values are given in Table 2; for comparative purposes we included in the table viscosity values of tetradecyl- and hexadecylcyclohexanes, as measured by Schmidt [2].

The viscosity of dodecylcyclohexane at temperatures selected by us was higher than that of 1,4-dihexylcyclohexane. The ratio of the viscosities of dibutyl- and monooctylcyclohexanes is not constant at different temperatures. Graphically, this relationship could be represented by two intersecting lines. Figure 2 shows the graphic relationship of the log of viscosity and the temperature. Within the limits of the temperatures studied

TABLE 1  
Di- and Monoalkylcyclohexanes

Nos.	Hydrocarbon	Melting point	Boiling point (pressure in mm)	$n_D^{20}$	$d_4^{20}$	MRD		$\Delta MRD$	Found % <sup>a</sup>	
						calcd.	found		C	H
(I)	n-C <sub>4</sub> H <sub>9</sub> -  -C <sub>4</sub> H <sub>9</sub> -n	—	118—120° (10)	1.4512	0.8159	64.91	64.78	0.13	85.75, 85.60	14.22, 14.17
(II)	n-C <sub>6</sub> H <sub>11</sub> -  -C <sub>6</sub> H <sub>11</sub> -n	—	140—141 (13)	1.4543	0.8204	74.21	74.12	0.09	85.70, 85.78	14.26, 14.43
(III)	n-C <sub>8</sub> H <sub>13</sub> -  -C <sub>8</sub> H <sub>13</sub> -n	9.5°	153—155 (4)	1.4560	0.8231	83.51	83.38	0.13	85.63, 85.90	14.24, 14.30
(IV)	n-C <sub>7</sub> H <sub>15</sub> -  -C <sub>7</sub> H <sub>15</sub> -n	23.5	170—171 (4)	1.4588	0.8269	92.80	92.70	0.10	85.30, 85.84	14.24, 14.10
(V)	n-C <sub>9</sub> H <sub>17</sub> -  -C <sub>9</sub> H <sub>17</sub> -n **	34.1	198—200 (4)	1.4490	0.8109	102.10	102.04	0.06	85.86, 85.62	14.22, 14.16
(VI)	n-C <sub>9</sub> H <sub>19</sub> -  -C <sub>9</sub> H <sub>19</sub> -n **	44.5	205—207 (3)	1.4511	0.8147	111.40	111.27	0.13	85.80, 85.53	14.55, 14.31
(VII)	iso-C <sub>8</sub> H <sub>11</sub> -  -C <sub>8</sub> H <sub>11</sub> -iso	—	94—95 (2)	1.4507	0.8143	74.21	74.16	0.05	85.51, 85.57	14.34, 14.28
(VIII)	 -C <sub>6</sub> H <sub>17</sub> -n ***	—	90.5—91 (2)	1.4515	0.8167	64.91	64.80	0.11	—	—
(IX)	 -C <sub>12</sub> H <sub>25</sub> -n ****	—	160—162 (5)	1.4570	0.8228	83.51	83.56	-0.05	—	—

<sup>a</sup> For compounds (I-VII) with general formula C<sub>n</sub>H<sub>2n</sub>, calculated %: C 85.63; H 14.37.

\*\* Values  $n_D^{20}$  and  $d_4^{20}$  cited.

\*\*\* Literature data [5]: b, p. 117—119° (11 mm);  $n_D^{20}$  1.4507,  $d_4^{20}$  0.8150.

\*\*\*\* Literature data [2]: b, p. 131—132° (0.8 mm),  $n_D^{20}$  1.4580,  $d_4^{20}$  0.8250.

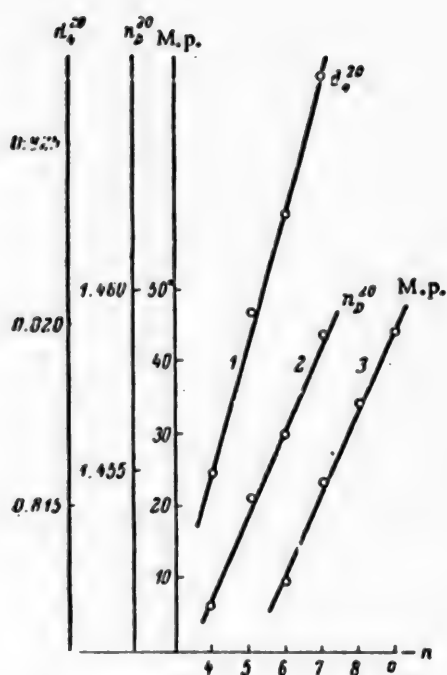


Fig. 1. The dependency of the physical constants of 1,4-dialkylcyclohexanes on the number of carbon atoms ( $n$ ) in the alkyl radical.

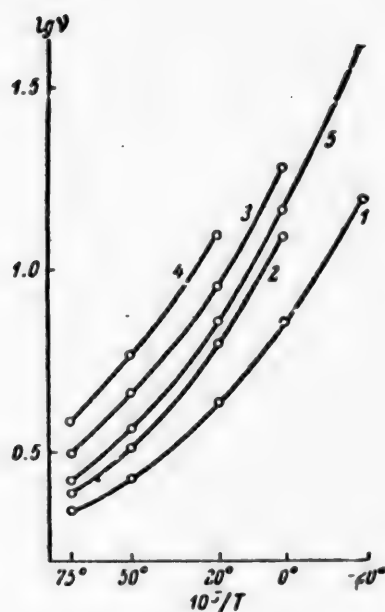


Fig. 2. Dependency of the log of the viscosity of 1,4-dialkylcyclohexanes on temperature ( $T$  = absolute temp.); 1) dibutylcyclohexane; 2) diamylcyclohexane; 3) dihexylcyclohexane; 4) diheptylcyclohexane; 5) diisooamylcyclohexane.

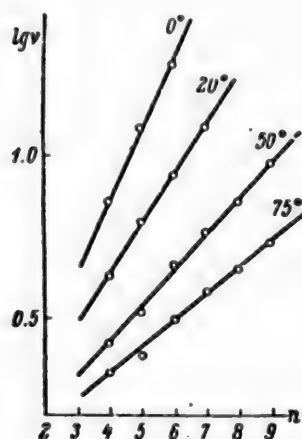


Fig. 3. Dependence of the log of the viscosity of 1,4-dialkylcyclohexanes on number of carbon atoms ( $n$ ) in the alkyl radical.

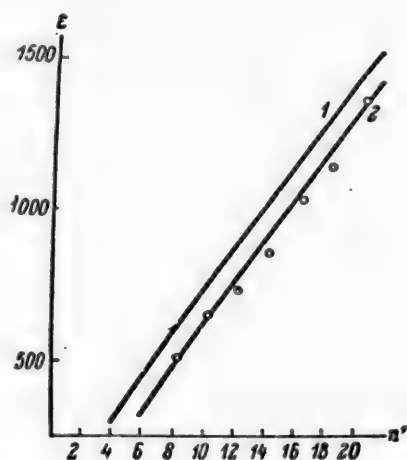


Fig. 4. Dependence of molar extinction ( $\epsilon$ ) coefficient of band  $2925 \text{ cm}^{-1}$  on number of  $\text{CH}_2$  groups ( $n'$ ) in the 1,4-dialkylcyclohexanes. 1) Monoalkylcyclohexanes; 2) dialkylcyclohexanes.

TABLE 2

Kinematic Viscosity of Di- and Monoalkylcyclohexanes

Nos.	Hydrocarbon	Viscosity (in centistokes)					
		-40°	-20°	0°	20°	50°	75°
(I)	$n\text{-C}_4\text{H}_9\text{--}\langle\text{H}\rangle\text{--C}_4\text{H}_9\text{-}n$	59.14	15.69	7.32	4.30	2.67	2.18
(II)	$n\text{-C}_5\text{H}_{11}\text{--}\langle\text{H}\rangle\text{--C}_5\text{H}_{11}\text{-}n$	—	—	12.39	6.31	3.25	2.44
(III)	$n\text{-C}_6\text{H}_{13}\text{--}\langle\text{H}\rangle\text{--C}_6\text{H}_{13}\text{-}n$	—	—	19.29	9.07	4.52	3.13
(IV)	$n\text{-C}_7\text{H}_{15}\text{--}\langle\text{H}\rangle\text{--C}_7\text{H}_{15}\text{-}n$	—	—	—	12.41	5.87	3.87
(V)	$n\text{-C}_8\text{H}_{17}\text{--}\langle\text{H}\rangle\text{--C}_8\text{H}_{17}\text{-}n$	—	—	—	—	7.21	4.34
(VI)	$n\text{-C}_9\text{H}_{19}\text{--}\langle\text{H}\rangle\text{--C}_9\text{H}_{19}\text{-}n$	—	—	—	—	9.60	5.37
(VII)	$\text{iso-C}_5\text{H}_{11}\text{--}\langle\text{H}\rangle\text{--C}_5\text{H}_{11}\text{-iso}$	273.99	42.39	14.69	7.20	3.68	2.64
(VIII)	$\langle\text{H}\rangle\text{--C}_8\text{H}_{17}\text{-}n$	—	15.85	7.45	4.53	2.64	2.17
(IX)	$\langle\text{H}\rangle\text{--C}_{12}\text{H}_{25}\text{-}n$	—	—	—	9.27	4.54	3.18
(X)	$\langle\text{H}\rangle\text{--C}_{14}\text{H}_{29}\text{-}n$ [2]	—	—	—	—	5.70	—
(XI)	$\langle\text{H}\rangle\text{--C}_{16}\text{H}_{33}\text{-}n$ [2]	—	—	—	—	7.49	—

TABLE 3

Infrared Spectral Data on Number of CH<sub>2</sub> and CH<sub>3</sub> Groups in Di- and Monoalkylcyclohexanes

Compound No.	Hydrocarbon	$\nu_{\text{CH}_2}$ , 2925 cm <sup>-1</sup>	Number of CH <sub>2</sub>	$\nu_{\text{CH}_3}$ , 2967 cm <sup>-1</sup>	Number of CH <sub>3</sub>	CH <sub>2</sub> tors, cm <sup>-1</sup>
(I)	$n\text{-C}_4\text{H}_9\text{--}\langle\text{H}\rangle\text{--C}_4\text{H}_9\text{-}n$	675	10	230	2	740
(II)	$n\text{-C}_5\text{H}_{11}\text{--}\langle\text{H}\rangle\text{--C}_5\text{H}_{11}\text{-}n$	755	12	230	2	730
(III)	$n\text{-C}_6\text{H}_{13}\text{--}\langle\text{H}\rangle\text{--C}_6\text{H}_{13}\text{-}n$	880	14	210	2	730
(IV)	$n\text{-C}_7\text{H}_{15}\text{--}\langle\text{H}\rangle\text{--C}_7\text{H}_{15}\text{-}n$	1100	16	220	2	730
(V)	$n\text{-C}_8\text{H}_{17}\text{--}\langle\text{H}\rangle\text{--C}_8\text{H}_{17}\text{-}n$	1170	28	200	2	730, 750
(VI)	$n\text{-C}_9\text{H}_{19}\text{--}\langle\text{H}\rangle\text{--C}_9\text{H}_{19}\text{-}n$	1400	20	200	2	725, 730, 740
(VII)	$\text{iso-C}_5\text{H}_{11}\text{--}\langle\text{H}\rangle\text{--C}_5\text{H}_{11}\text{-iso}$	545	8	390	4	755
(VIII)	$\langle\text{H}\rangle\text{--C}_8\text{H}_{17}\text{-}n$	860	12	100	1	—
(IX)	$\langle\text{H}\rangle\text{--C}_{12}\text{H}_{25}\text{-}n$	1200	16	95	1	—



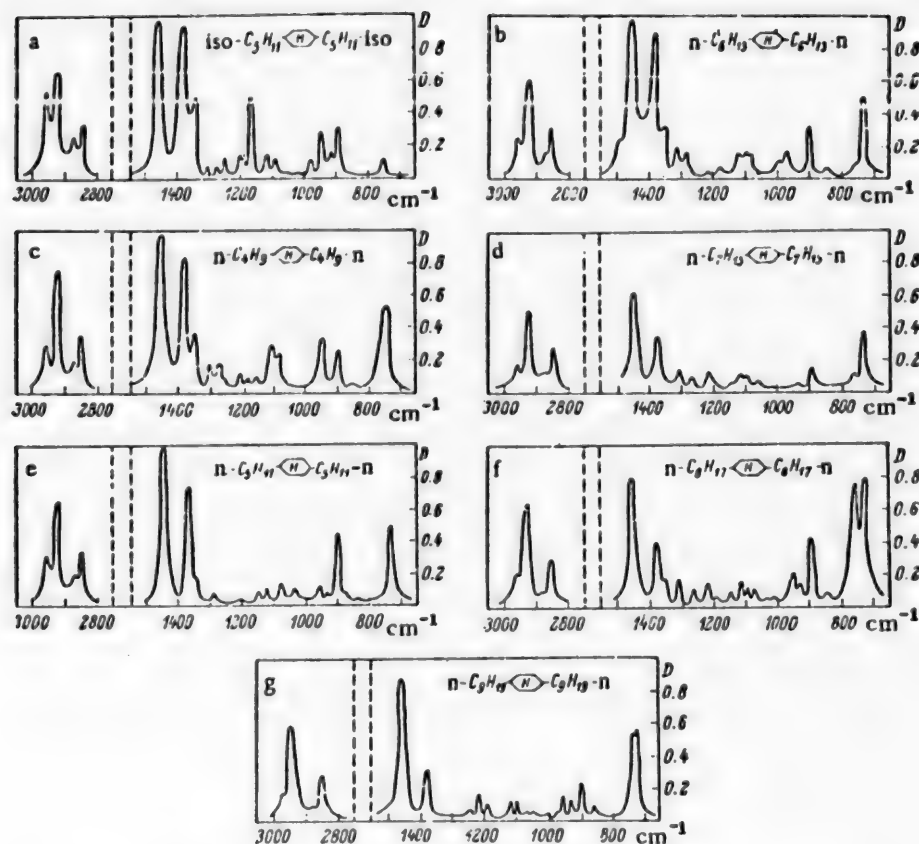


Fig. 5. Infrared spectra of 1,4-dialkylcyclohexanes in  $\text{CCl}_4$ . Concentrations (mg/10 ml  $\text{CCl}_4$ ): a) 25.5; b) 17.65; c) 23.8; d) 12.8; e) 18.8; f) 16.1; g) 13.3.

by us, the log of viscosity increased linearly with increased length of alkyl radicals in the transition from dibutyl- to dinonylcyclohexane. The linear relationship is shown in Fig. 3. All lines in the graph intersect in the origin of coordinates and can be expressed by the following equations:  $\log \nu_0^\circ = 0.217 n$ ,  $\log \nu_{20}^\circ = 0.158 n$ ,  $\log \nu_{50}^\circ = 0.109 n$ ,  $\log \nu_{75}^\circ = 0.082 n$ .

On an IKS-12 apparatus with NaCl prism we obtained infrared spectra of 1,4-dialkylcyclohexanes (I-VII) in the  $700\text{--}1500\text{ cm}^{-1}$  region. Compounds (I-IV, VII) were photographed in a layer 0.1 mm thick, and compounds (V) and (VI) pressed into KBr. Per 40 mg substance we used 2 g KBr. The aperture was changed according to the spectrum. In all of the spectra was found the  $720\text{--}730\text{ cm}^{-1}$  band, characteristic of the torsional vibration of the methylene groups ( $\nu_{\text{CH}_2}$  torsion). The displacement of this band toward greater frequency when the number of  $\text{CH}_2$  groups was reduced in an aliphatic chain (Table 3) agrees with previous data [6]. In dioctyl- and dinonylcyclohexanes the  $730\text{ cm}^{-1}$  band splits. An analogous phenomenon was observed earlier with spectra of substances in the crystalline state [7]. All spectra have intense  $1375$  and  $1450\text{ cm}^{-1}$  bands, characteristic, resp., of strained oscillations of the  $\text{CH}_3$  and  $\text{CH}_2$  groups. In the spectrum of diisoamylcyclohexane the band  $1375\text{ cm}^{-1}$  splits to  $1350$  and  $1385\text{ cm}^{-1}$ , which confirms the presence of branching [8]. In addition in all spectra we observed bands  $895$ ,  $950$ , and a doublet in the  $1100\text{ cm}^{-1}$  region. These are probably characteristic frequencies for the cyclohexane ring [9]. In order to determine the number of  $\text{CH}_2$  and  $\text{CH}_3$  groups in the compounds under consideration, they were photographed with a LiF prism in the  $2800\text{--}3000\text{ cm}^{-1}$  region. All compounds were photographed in  $\text{CCl}_4$  solution in a cuvette with constant layer thickness of 1 mm at  $0.135\text{ mm}$  incoming and outgoing aperture. The concentrations of the solutions ( $C = \text{mg substance}/10\text{ ml CCl}_4$ ) are shown in Fig. 5. The intensity of absorption bands  $2925\text{ cm}^{-1}$  ( $\text{CH}_2$ ) and  $2957\text{ cm}^{-1}$  ( $\text{CH}_3$ ) is linearly dependent on the number of normal groups, as was found with alkanes and alkylcyclohexanes [10]. Table 3 gives the values of molar extinction coefficients ( $\epsilon$ ) of bands  $2925$  and  $2957\text{ cm}^{-1}$ , and also the number of  $\text{CH}_2$ - and  $\text{CH}_3$  groups in the molecule as they correspond to those values. Figure 4 graphically expresses the dependency of  $\epsilon$  of band  $2925\text{ cm}^{-1}$  on the number of  $\text{CH}_2$  groups [2]. An analogous graph of dependency for monoalkylcyclohexanes is parallel to the one above, but 110 units higher.

## SUMMARY

1. When symmetrical p-dialkylbenzenes were hydrogenated, a number of 1,4-dialkylcyclohexanes with four to nine carbon atoms in the alkyl radicals were obtained.
2. The dependence of physical constants of 1,4-dialkylcyclohexanes on the number of carbon atoms in the alkyl radicals was studied.
3. The dependence of molar extinction coefficient of band  $2925\text{ cm}^{-1}$  on the number of  $\text{CH}_2$  groups in 1,4-dialkylcyclohexane molecules was studied by means of infrared spectra.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. Some or all of this periodical literature may well be available in English translation. A complete list of the cover-to-cover English translations appears at the back of this issue.

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# AN INVESTIGATION OF THE INTERACTION OF HYDRAZINE HYDRATE AND DIMETHYLHYDRAZINE WITH SOME OXIDES OF COMPOUNDS OF THE ACETYLENE SERIES

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We established in previous work [1] that it is possible to convert  $\alpha$ -aminoalcohols of the acetylene and vinylacetylene series into the corresponding pyrrole homologs. The purpose of the present work was investigation of the interaction of some oxides of compounds of the acetylene series with hydrazine hydrate and with dimethylhydrazine and also finding of the conditions under which hydrazinoalcohols can be transformed into N-aminopyrroles, i.e., development of a convenient method for preparing the latter. The necessity of carrying out an investigation on the subject was imposed by the circumstance that up to now no convenient and effective method for synthesizing this interesting type of compounds has been available. An attempt to synthesize N-aminopyrroles starting from  $\gamma$ -diketones, dicarboxylic acids, and hydrazine hydrate did not lead to the desired results [2, 3]. The poor yields in these reactions were due to a number of secondary processes. We subjected to investigation the oxides listed in Table 1.

Upon interaction of the oxide (I) with hydrazine hydrate and of oxide (II) with dimethylhydrazine, the corresponding hydrazinoalcohols (IV) and (V) were isolated and characterized; their properties are listed in Table 2.

Analysis of the infrared spectra of these compounds showed the presence of absorption bands characteristic for a triple bond (in the region of  $2170-2250\text{ cm}^{-1}$ ) and for a tertiary alcohol hydroxyl ( $1150\text{ cm}^{-1}$ ).

The compounds (IV) and (V) were converted into the corresponding N-aminopyrroles. The synthesis of the N-aminopyrroles, i.e., compounds (VI) - (IX) in Table 2, was carried out by a single-stage conversion. In the spectroscopic examination of the compounds prepared maxima were detected at  $1536$  and  $1145\text{ cm}^{-1}$ , which are characteristic for the pyrrole ring; at  $780$  and  $720\text{ cm}^{-1}$ , characteristic for CH groups; at  $3300\text{ cm}^{-1}$ , characteristic for the  $\text{NH}_2$  group; and finally at  $2962\text{ cm}^{-1}$ , characteristic for the  $\text{CH}_3$  group. The determinations were made on an IKS-11 infrared spectrometer with NaCl and LiF prisms.

On the basis of the data obtained one may consider it established that addition of hydrazine hydrate and dimethylhydrazine to the oxides mentioned above proceeds according to the Krasuskii rule, i.e., opening of the oxide ring takes place at the carbon to which the greatest number of hydrogen atoms are bound, while closing of the pyrrole ring proceeds as shown below:

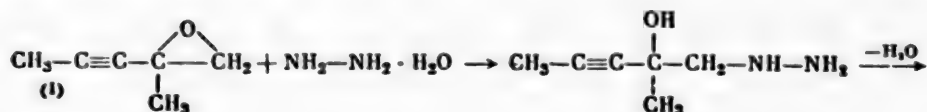
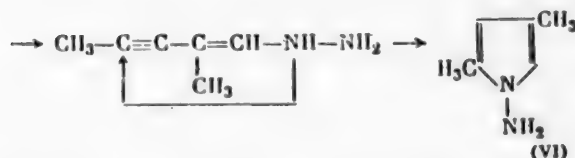


TABLE 1

No. of compound	Formula	Name of compound	B.p. (pressure in mm)	$d_4^{20}$	$n_D^{20}$
(I)	$\text{CH}_3-\text{C}\equiv\text{C}-\text{C}(\text{CH}_3)-\text{CH}_2-\text{O}$	2-methyloxido-1,2-pentyne-3	40–41° (22)	0.9264	1.4461
(II)	$\text{C}_4\text{H}_9-\text{C}\equiv\text{C}-\text{C}(\text{CH}_3)-\text{CH}_2-\text{O}$	2-methyloxido-1,2-octyne-3	48–49 (2–3)	0.8777	1.4474
(III)	$\text{C}_6\text{H}_5-\text{C}\equiv\text{C}-\text{C}(\text{CH}_3)-\text{CH}_2-\text{O}$	2-methyl-4-phenyloxido-1,2-butyne-3	108–109 (8)	1.0278	1.5552



One must note that the velocity of the conversion of hydrazinoalcohols into the corresponding aminopyrroles is considerably lower than that of the conversion of hydroxyaminoalcohols.

It was found that the velocity of the reaction of the oxides mentioned above with hydrazine hydrate varies greatly depending on the nature of the radical R which substitutes an acetylene hydrogen.

For instance, oxide (I) reacts with hydrazine hydrate with a considerable evolution of heat, while the oxides (II) and (III) add hydrazine hydrate only after prolonged heating. This difference in the velocities of the formation of hydrazinoalcohols is apparently due primarily to a sharp reduction of the mutual solubility of the reacting substances and only to a lesser extent to the structural characteristics of the oxides.

#### EXPERIMENTAL

Hydrazino-1,2-methylpentyn-3-ol-2 (IV). Into a three-necked flask equipped with a reflux condenser and an agitator and containing a double (100%) excess of hydrazine hydrate (35 g), 33 g of 2-methyloxido-1,2-pentyne-3 (I) was added under agitation. The reaction took place with the evolution of a considerable amount of heat. The reaction mixture was heated for 3 hr. on a water bath and then distilled in vacuum. The substance obtained (IV) crystallized in white needles which were found to be soluble in most organic solvents and in hot water.

Found %: C 56.20; H 9.37; N 21.91.  $\text{C}_6\text{H}_{12}\text{ON}_2$ . Calculated %: C 56.25; H 9.38; N 21.87.

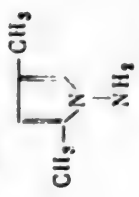
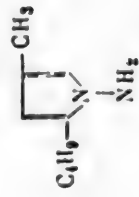
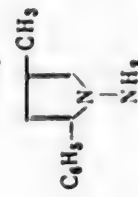
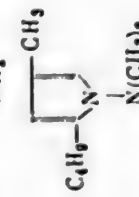
N-Amino-2,4-dimethylpyrrole (VI). 15 g of hydrazino-1,2-methylpentyn-3-ol-2 (VI) together with several drops of hydrazine hydrate and 1–2 drops of quinoline was heated for 3 days at 170–180° in a sealed tube placed in an oil bath. The substance that had been separated crystallized after two distillations in vacuum. The yield was 47%.

Found %: C 65.40; H 9.18; N 25.52.  $\text{C}_6\text{H}_{10}\text{N}_2$ . Calculated %: C 65.42; H 9.15; N 25.43.

The mercury derivative of (VI) decomposed at 110–111°.

N-Amino-2-methyl-4-butylpyrrole (VII). 15 g of hydrazine hydrate and 20 g of 2-methyloxido-1,2-octyne-3 (II) were heated under constant agitation in a flask on an oil bath for 3 days at 150°. After vacuum

TABLE 2

No. of compound	Formula	Name of compound	B.p. (pressure in mm)	$n_D^{20}$	$d_4^{20}$	MR,	
						calcd.	found
(IV)	$\text{CH}_3-\text{C}\equiv\text{C}-\text{COH}-\underset{\text{CH}_3}{\text{CH}}-\text{NH}-\text{NH}_2$	hydrazino-1,2-methylpentyn-3-ol-2	m.p. 65°	—	—	—	—
(V)	$\text{C}_4\text{H}_9-\text{C}\equiv\text{C}-\text{COH}-\underset{\text{CH}_3}{\text{CH}}-\text{NH}-\text{N}(\text{CH}_3)_2$	N-dimethylhydrazino-1,2-methyloctyn-3-ol-2	84—85° (0.5)	1.4642	0.9245	60.17	59.4
(VI)		N-amino-2-methyl-4-butylpyrrole	m.p. 26—27	—	—	—	—
(VII)		N-amino-2-methyl-4-butylpyrrole	85—86 (0.3)	1.4990	0.9492	44.52	44.11
(VIII)		N-amino-2-methyl-4-phenylpyrrole	m.p. 42—43	—	—	—	—
(IX)		N-dimethylamino-2-methyl-4-butylpyrrole	54—56 (0.3)	1.4811	0.8829	57.504	57.2

distillation the substance that had been separated was a colorless liquid with a penetrating odor. This substance gave the typical reactions for a pyrrole.

Found %: C 70.51; H 10.41; N 18.32.  $C_9H_{10}N_2$ . Calculated %: C 70.7; H 10.40; N 18.42.

N-Amino-2-methyl-4-phenylpyrrole (VIII). 15 g of hydrazine hydrate and 23 g of 2-methyl-4-phenyloxido-1,2-butyne-3 (II) to which 1 ml of quinoline had been added were heated in a round-bottomed flask under constant stirring on an oil bath for 4 days at 180°. After distillation in vacuum a very viscous substance with a b. p. 125-126° (0.3 mm) was separated which had a penetrating odor resembling that of almond. M. p. 42-43°, yield 52%.

Found %: C 76.48; H 6.99; N 16.38.  $C_{11}H_{12}N_2$ . Calculated %: C 76.63; H 6.97; N 16.27.

The mercury derivative melted with decomposition at 137-138°.

N-Dimethylhydrazino-1,2-methyloctyn-3-ol-2 (V). 12 g of 2-methyloxido-1,2-octyne-3 (II) and 15 g of hydrazine hydrate (a 100% excess) placed into a flask were heated on a water bath for 3 days under agitation, whereupon distillation was carried out. Yield 79.4%.

Found %: C 66.48; H 11.21;  $H_{act}$  0.98.  $C_7H_{23}ON_2$ . Calculated %: C 66.6; H 11.1;  $H_{act}$  1.

N-Dimethylamino-2-methyl-4-butylpyrrole (IX). 15 g of dimethylhydrazino-1,2-methyloctyn-3-ol-2 (V) to which a drop of quinoline had been added was heated on an oil bath for 2 days at 150°. As a result of vacuum distillation the substance (IX) was isolated. Yield 42.75%.

Found %: C 73.29; H 10.68; N 15.48.  $C_{11}H_{20}N_2$ . Calculated %: C 73.26; H 10.63; N 15.56.

An azodyestuff was prepared in the usual manner by coupling with phenyldiazonium chloride; m. p. 159-160° (decomp.).

#### SUMMARY

1. As a result of the action of hydrazine hydrate and dimethylhydrazine on oxides of compounds of the acetylene series, the oxide ring opens at the carbon atom to which the greatest number of hydrogen atoms are bound.

2. A new method has been developed for the synthesis of N-aminopyrroles. The following N-aminopyrroles not described in the literature before were synthesized by this method: N-amino-2,4-dimethylpyrrole, N-amino-2-methyl-4-butylpyrrole, N-amino-2-methyl-4-phenylpyrrole, and N-dimethylamino-2-methyl-4-butylpyrrole.

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# AN INVESTIGATION IN THE FIELD OF DIOXIDES OF COMPOUNDS OF THE ACETYLENE SERIES; PART II

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We established in a preceding investigation [1] that interaction of dioxides of compounds of the acetylene series with primary aliphatic amines results in the formation of acetylenic diaminoglycols, which on heating are converted into the corresponding  $\beta$ -aminopyrrolecarbinols.

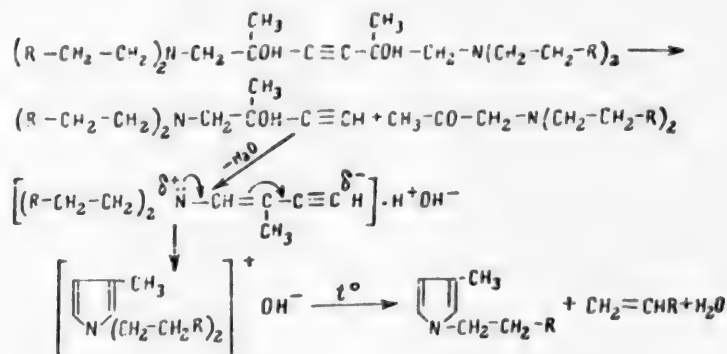
The purpose of the work reported in this instance was investigation of the interaction of acetylenic dioxides with secondary aliphatic amines. It was of interest to establish in what manner the oxide ring opens under the action of secondary amines, to compare the velocities of the interaction of dioxides with primary and secondary amines, and to investigate the relative stability of the diaminoglycols that are formed.

The interaction of 2,5-dimethyl-dioxido-1,2; 5,6-hexyne-3 (I) with diethylamine and dipropylamine was investigated. As products of the reactions in question the following diaminoglycols were isolated: 1,6-di-(diethylamino)-2,5-dimethylhexyn-3-diol-2,5 (II); 1,6-di-(dipropylamino)-2,5-dimethylhexyn-3-diol-2,5 (III) (see the following table).

No. of compound	Formula	B.p. (pressure in mm)	$n_D^{20}$	$d_4^{20}$	M <sub>r</sub>	
					found	calcd.
(I)		95-96 (12)	1.4665	—	—	—
(II)		117-118 (0.5)	1.4646	0.9239	85.05	85.02
(III)		145-147 (2)	1.4675	0.9121	103.65	103.49
(IV)		54-55 (21)	1.4781	0.8807	35.04	35.33
(V)		52-53 (11)	1.4747	0.8760	39.48	39.95

It was found that the velocity of the interaction of the dioxides with secondary amines is lower than that with primary amines. For instance, the reaction with monoethylamine takes place at room temperature, with evolution of heat, while that with diethylamine can be completed only by heating the reaction mixture in a sealed tube at 100° for 7-8 hr. It was established that the diaminoglycols (II) and (III) split on heating, with the formation of an olefin, an aminoketone, and a pyrrole. The olefins which formed were identified as their dibromoderivatives. The aminoketones were identified by analysis and by the preparation of the corresponding semicarbazones. From the pyrroles azodyestuffs and their picrates were prepared.

Thus, N-disubstituted diaminoglycols on heating undergo other transformations than N-monosubstituted diaminoglycols. The latter are converted directly into  $\beta$ -aminopyrrolecarbinols. In the case of the N-disubstituted diaminoglycols, this reaction becomes difficult because of the absence of active hydrogen in the amino group, so that the reaction of splitting of diaminoglycols predominates, which apparently proceeds as formulated below:



One must assume that all of the processes formulated take place simultaneously.

#### EXPERIMENTAL

**Preparation of 1,6-di-(diethylamino)-2,5-dimethylhexyn-3-diol-2,5 (II).** 20 g of the dioxide (I) and 30 g of diethylamine were heated for 10 hr in a sealed tube placed in a boiling water bath. After a double distillation in high vacuum, 36 g of a viscous pale yellow liquid was separated which dissolved in water and in organic solvents.

Found %: C 67.69; H 11.31; N 9.77; act. H 1.90.  $\text{C}_{16}\text{H}_{32}\text{O}_2\text{N}_2$ . Calculated %: C 67.57; H 11.35; N 9.85; act. H 2.

**Splitting of diaminoglycol (II).** 35 g of (II) were distilled at atmospheric pressure. When the temperature of the bath reached 180°, violent evolution of gas and distillation of a turbid mobile liquid began and continued for 1.5 hr. 26 g of liquid products and 1.5 liters of gas were isolated. The liquid was treated several times with a 40% aqueous solution of sodium bisulfite. The bisulfite extracts were combined and worked up separately (see below), while the remaining product was dried with calcined  $\text{MgSO}_4$  and distilled in vacuum. In this manner 9 g of N-ethyl-3-methylpyrrole (IV) was isolated in the form of a mobile transparent liquid, the physical properties of which are given in the table. This substance is insoluble in water but readily soluble in organic solvents; it gives the characteristic reactions of a pyrrole.

Found %: C 76.62; H 10.30; N 12.68.  $\text{C}_7\text{H}_{11}\text{N}$ . Calculated %: C 77.06; H 10.09; N 12.85.

To 3 g of freshly distilled aniline dissolved in 30 ml of water and 8.4 ml of concentrated HCl a solution of 2.4 g of  $\text{NaNO}_2$  in 12 ml of water was added dropwise (the temperature of the reaction mixture must not be allowed to rise above 0°). To the diazonium salt that had formed a solution of 3 g of the pyrrole (IV) in 30 ml of alcohol was added. There was a sudden and pronounced reddening of the solution accompanied by separation at the bottom of oily drops of a dark red color. The dyestuff was extracted with ether. The ether solution was dried with  $\text{MgSO}_4$ . The ether was distilled off and the product distilled in vacuum. In this manner 3.5 g of a bright red liquid was isolated which was insoluble in water, but readily soluble in ether and alcohol.

B. p. 126-127° (1 mm),  $d_4^{20}$  1.0383. Found %: N 19.40.  $C_{13}H_{15}N_3$ . Calculated %: N 19.70.

With picric acid in an aqueous-etheral solution this substance formed a picrate which had a decomposition point of 110° after being crystallized from alcohol.

The combined bisulfite extracts obtained by treatment of the liquid products of splitting of the diamino-glycol (II) were saturated with KOH. The upper layer that separated was dried with  $MgSO_4$  after being separated from the aqueous solution. On distillation in vacuum 14 g of a transparent mobile liquid was isolated, the physical constants of which corresponded in every respect to data for diethylaminoacetone published in the literature [2].

B. p. 57-58° (16 mm),  $n_D^{20}$  1.4250,  $d_4^{20}$  0.8627.

Found %: C 65.02; H 11.77; N 10.69.  $C_7H_{13}ON$ . Calculated %: C 65.07; H 11.70; N 10.84.

With semicarbazide hydrochloride in an aqueous alcohol solution (after an equivalent quantity of NaOH had been added) the substance yielded a semicarbazone forming white needles with a m. p. = 143° on recrystallization from benzene. A sample of the product obtained did not show any depression of the melting point on being mixed with the semicarbazone of diethylaminoacetone.

The gaseous products of splitting were investigated by absorption gas analysis and combustion. The composition of the gas mixture that had been isolated was as follows (in %): olefins - 56, air - 36, hydrogen - 4, acetylene - 3, saturated hydrocarbons - 1.

On being freed of acetylene by absorption with Plosovay reagent, the gas was subjected to bromination. The product that was isolated had constants corresponding in every respect to data published in the literature for dibromoethane.

B. p. 128-129°,  $n_D^{20}$  1.5382,  $d_4^{20}$  2.1780. Found %: Br 85.37.  $C_2H_4Br_2$ . Calculated %: Br 85.11.

Preparation of 1,6-di-(dipropylamino)-2,5-dimethylhexyn-3-diol-2,5 (III). 30 g of dioxide (I) and 47 g of dipropylamine were heated for 25 hr at 120° in a sealed tube placed in an oil bath. After two distillations in high vacuum 21 g of a viscous liquid was isolated which was soluble in water and in organic solvents.

Found %: C 70.57; H 11.78; N 8.15; act. H 1.88.  $C_{18}H_{36}O_2N_2$ . Calculated %: C 70.53; H 11.84; N 8.23; act. H 2.

Splitting of diaminoglycol (III). 20 g of (III) were subjected to distillation at atmospheric pressure. Splitting took place at 200-250° and continued for a period of 4 hr. Fifteen grams of liquid and 0.1 liter of gas were isolated. Analysis of the products of splitting was conducted as described above. On distillation in vacuum 5 g of N-propyl-3-methylpyrrole (V) was isolated, the physical characteristics of which are given in the table. This is a transparent mobile liquid which does not dissolve in water, but dissolves with facility in organic solvents. It gives the characteristic reactions of a pyrrole.

Found %: C 78.11; H 10.49; N 11.29.  $C_8H_{13}N$ . Calculated %: C 77.98; H 10.65; N 11.37.

By using the method described above, an azodyestuff was obtained in the form of a light-red liquid which was insoluble in water, but dissolved readily in ether and alcohol. Because it oxidized rapidly in the air, no consistent analytical results could be obtained; b. p. 141-142° (2 mm),  $d_4^{20}$  1.0352. With picric acid in an aqueous-etheral solution this substance formed a picrate which consisted of large prismatic crystals of a dark blue color; on recrystallization from alcohol the picrate melted at 95-96°.

Found %: N 18.60.  $C_{14}H_{17}N_3 \cdot C_6H_3O_7N_3$ . Calculated %: N 18.42.

Treatment of the bisulfite compound with KOH and subsequent distillation in vacuum yielded 8 g of a mobile transparent liquid the physical constants of which corresponded in every respect to data published for dipropylaminoacetone [3].

B. p. 53-54° (5 mm),  $n_D^{20}$  1.4297,  $d_4^{20}$  0.8563. Found %: C 69.00; H 12.22; N 8.87.  $C_9H_{19}ON$ . Calculated %: C 68.73; H 12.18; N 8.98.

With semicarbazide hydrochloride in an aqueous alcohol solution (after addition of an equivalent amount of NaOH) the substance yielded a semicarbazone - white platelets with a m. p. = 145° on recrystallization from benzene.

The gas which evolved during the splitting of (III) was subjected to bromination.

The 1,2-dibromopropane that formed had physical characteristics which corresponded fully to published data.

B. p. 140-141°,  $n_D^{20}$  1.5206,  $d_4^{20}$  1.9325. Found %: Br 79.30.  $C_3H_6Br_2$ . Calculated %: Br 79.21.

#### SUMMARY

It was shown that reaction of 2,5-dimethyl-dioxido-1,2; 5,6-hexyne-3 with secondary amines produces tertiary acetylenic diaminoglycols, which upon heating are split, forming the corresponding dialkylaminoketones, N-substituted pyrrole homologues, and olefins.

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2. Magee, Hensze, J. Am. Chem. Soc. 60, 2148 (1938).

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. Some or all of this periodical literature may well be available in English translation. A complete list of the cover-to-cover English translations appears at the back of this issue.

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# INTERACTION OF PHOSPHORUS ACID CHLORIDES WITH BIFUNCTIONAL ORGANIC COMPOUNDS.

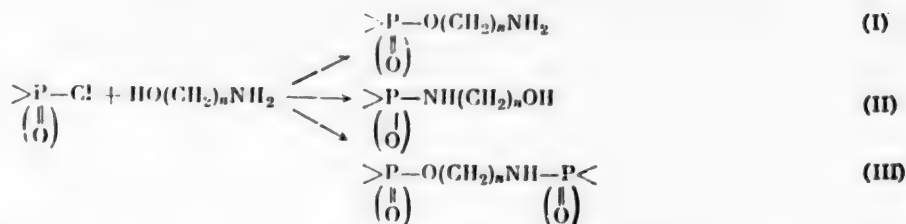
## I. INTERACTION OF CHLORIDES OF PHOSPHORUS ACIDS WITH FATTY HYDROXYAMINES

M. A. Sokolovskii and P. M. Zavlin

Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 11, pp. 3562-3565,  
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A large number of publications deal with the interactions into which alcohols and amines enter with chlorides of phosphorus acids. The reactions in question, as is known, lead to the formation of esters in the first case [1] and of anilides of the corresponding phosphorus acids in the second case [2]. As far as the nature of the interaction of aminoalcohols with chlorides of phosphorus acids is concerned, no information on the reactions involved has been given in the literature hitherto. In investigating the direction which the reaction of chlorides of phosphorus acids may take when the other reacting substance is an aminoalcohol, i.e., a compound containing two nucleophilic groups (a hydroxy group and an amino group), one must take into consideration quite generally the possibility that either the hydroxy or the amino group may react and also the additional possibility that both of these functional groups may react simultaneously, in accordance with the scheme indicated below:



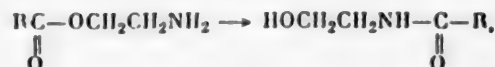
An investigation of the reactions formulated above which was undertaken by us indicated that under certain conditions pertaining to the ratio of the reacting substances and the temperature only the first direction of the reaction scheme shown is realized. Thus, the interaction of ethanolamine with phosphorus oxychloride at a stoichiometric ratio of the reacting substances and a temperature no higher than 90° led to the formation of the trihydrochloride of the tri-(β-aminoethyl ester) of phosphoric acid with a yield close to the theoretical according to the following equation:



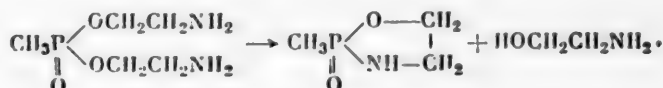
Phosphorus trichloride, the dichloride of methylphosphinic acid, the dichloride of phenylphosphinic acid, and the dichloride of p-chlorophenylphosphinic acid react with ethanolamine in the same manner. The reaction of phosphorus acid chlorides with hexanolamine-1,6\* proceeds in the same direction. The composition of the products obtained was confirmed by the results of elementary analysis.

\* The hexanolamine-1,6 was kindly supplied by P. A. Moshkin and E. A. Preobrazhenskii, for which the authors thank them.

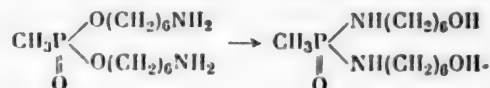
The free bases were prepared from the hydrochlorides. Potentiometric titration and analysis according to Van Slyke confirmed the presence of primary amino groups in the products obtained. As far as the properties of the new compounds are concerned, one must note that in contradistinction to the lability of O-acyl derivatives of ethanolamine, which have a tendency to isomerize spontaneously into N-acyl derivatives [3],



the phosphorus acyl aminoalcohols are stable under ordinary conditions. However, one must bear in mind that, depending on the constitution of the initial hydroxyamines, the phosphorus-containing amines which are obtained may undergo at high temperature (of the order of 150° or higher) cyclization in the case of a short carbon chain of the initial aminoalcohol, as has been shown on the example of the di-(β-aminoethyl ester) of methylphosphinic acid.



or partial regrouping from O-derivatives to N-derivatives in the case of a long carbon chain of the initial aminoalcohol, as has been shown on the example of the di-(ω-aminoethyl ester) of methylphosphinic acid:



Investigation of the interactions of aminoalcohols with the chlorides of phosphorus acids made it possible to synthesize a new group of organophosphorus compounds with two or three amino groups [4], which may serve as initial di- or triamine monomers for the preparation of high-molecular compounds containing phosphorus.

Furthermore, the results obtained in this research gave rise to the expectation that the interaction of phosphorus acid chlorides with alcohols in the presence of primary amines would also lead to the formation of phosphorus acid esters, with the primary amines functioning solely as acceptors of hydrogen chloride, according to the equation formulated below for the case of phosphorus trichloride and ethyl alcohol:



where R is an alkyl or aryl.

Experiments along this line which have been carried out confirmed fully the correctness of this assumption. The interaction of various alcohols with phosphorus trichloride in the presence of primary amines resulted in the formation of a number of phosphites, which were obtained with good yields [5].

#### EXPERIMENTAL

Trihydrochloride of the tri-(β-aminoethyl ester) of phosphoric acid. Into a three-necked flask equipped with an agitator, a thermometer, a dropping funnel, and a reflux condenser, 18.3 g (0.3 mol) of freshly distilled ethanolamine (d 1.022) was placed. With agitation at a low temperature 15.3 g (0.1 mol) of freshly distilled phosphorus oxychloride was added at such a rate that the temperature of the reaction mixture did not rise above 90°. The reaction was completed in 1.5-2 hr. The product obtained was washed with benzene; it crystallized on being boiled in absolute alcohol. M. p. 212-213°.

Found %: C 21.56; H 6.64; N 12.70 (Van Slyke); N 12.9; Cl 30.8; P 9.7.  $\text{C}_8\text{H}_{21}\text{O}_4\text{N}_3\text{PCl}_3$ . Calculated %: C 21.41; H 6.32; N 12.45; Cl 31.6; P 9.2.

Tri-(β-aminoethyl ester) of phosphoric acid. To 15 g of the trihydrochloride of the tri-(β-aminoethyl ester) of phosphoric acid was added under agitation an alcohol solution of sodium alcoholate prepared by



dissolving 3.1 g of metallic sodium in 100 ml of absolute alcohol. Precipitation of sodium chloride took place during 2-3 hr, with a slight evolution of heat. The free base that was formed went into solution. The sodium chloride was filtered off and the alcohol evaporated. The free base (8 g) was obtained in the form of a yellow viscous liquid with an amine odor. Yield 80%.

Found %: N 18.1 (Van Slyke); P 13.5, M 238.  $C_8H_{18}O_4N_3P$ . Calculated %: N 18.5; P 13.65, M 233.

The synthesis of a number of other phosphorus-containing di- and triamines was carried out similarly. Data obtained by elementary analysis of the compounds prepared are listed in the table.

Formula	Name of compound	Found %		Calcd. %	
		N (Van Slyke)	P	N	P
$P(OC_2H_4NH_2 \cdot HCl)_3$	Trihydrochloride of tri( $\beta$ -aminoethyl ester) of phosphorous acid	12.7, 13.2	9.05, 9.15	13.1	9.6
$CH_3P(OC_2H_4NH_2 \cdot HCl)_2$ $\parallel$ O	Dihydrochloride of di( $\beta$ -aminoethyl ester) of methylphosphinic acid	10.7	11.9, 12.4	10.9	12.12
$CH_3P(OC_2H_4NH_2)_2$ $\parallel$ O	Di( $\beta$ -aminoethyl ester) of methylphosphinic acid	15.7	17.3	15.25	16.95
$C_6H_5P(OC_2H_4NH_2 \cdot HCl)_2$ $\parallel$ O	Dihydrochloride of di( $\beta$ -aminoethyl ester) of phenylphosphinic acid	8.5, 8.7	10.0, 9.9	9.91	9.78
$C_6H_5P(OC_2H_4NH_2)_2$ $\parallel$ O	Di( $\beta$ -aminoethyl ester) of phenylphosphinic acid	11.30, 11.20	12.5, 12.6	11.45	12.70
$p\text{-ClC}_6H_4P(OC_2H_4NH_2 \cdot HCl)_2$ $\parallel$ O	Dihydrochloride of di( $\beta$ -aminoethyl ester) of p-chlorophenylphosphinic acid	7.8, 7.7	8.5, 8.6	7.96	8.82
$p\text{-ClC}_6H_4P(OC_2H_4NH_2)_2$ $\parallel$ O	Di( $\beta$ -aminoethyl ester) of p-chlorophenylphosphinic acid	9.93	11.0	10.05	11.12
$CH_3P(OC_6H_{12}NH_2 \cdot HCl)_2$ $\parallel$ O	Dihydrochloride of di( $\omega$ -aminohexyl ester) of methylphosphinic acid	7.65, 7.8	8.6, 8.9	7.65	8.45
$CH_3P(OC_6H_{12}NH_2)_2$ $\parallel$ O	Di( $\omega$ -aminohexyl ester) of methylphosphinic acid	9.3	10.85	8.9	10.5
$C_6H_5P(OC_6H_{12}NH_2 \cdot HCl)_2$ $\parallel$ O	Dihydrochloride of di( $\omega$ -aminohexyl ester) of phenylphosphinic acid	6.4, 6.63	7.2, 7.3	6.53	7.22
$C_6H_5P(OC_6H_{12}NH_2)_2$ $\parallel$ O	Di( $\omega$ -aminohexyl ester) of phenylphosphinic acid	7.57, 7.7	8.5, 8.6	7.86	8.7
$p\text{-ClC}_6H_4P(OC_6H_{12}NH_2 \cdot HCl)_2$ $\parallel$ O	Dihydrochloride of di( $\omega$ -aminohexyl ester) of p-chlorophenylphosphinic acid	6.15, 6.20	6.6, 6.8	6.05	6.7
$p\text{-ClC}_6H_4P(OC_6H_{12}NH_2)_2$ $\parallel$ O	Di( $\omega$ -aminohexyl ester) of p-chlorophenylphosphinic acid	7.30, 7.40	7.8, 7.7	7.16	7.94

E. I. Klyachko collaborated in the experimental part of the investigation.

#### SUMMARY

1. The reactions of different phosphorus acid chlorides with fatty hydroxyamines were investigated.
2. It was established that at stoichiometric ratios of the reacting substances and temperatures no higher than 90°, the chlorides of phosphorus acids react with fatty hydroxyamines exclusively at the hydroxy group of the latter.

3. Eight phosphorus-containing di- and triamines that had not been reported before were synthesized.

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# INVESTIGATION OF CYANOETHYLATION IN A SERIES OF NITROGENOUS HETEROCYCLES

## II. CYANOETHYLATION OF 5(6)-NITRO- AND 2-METHYL-5(6)-NITROBENZIMIDAZOLES

A. M. Éfros

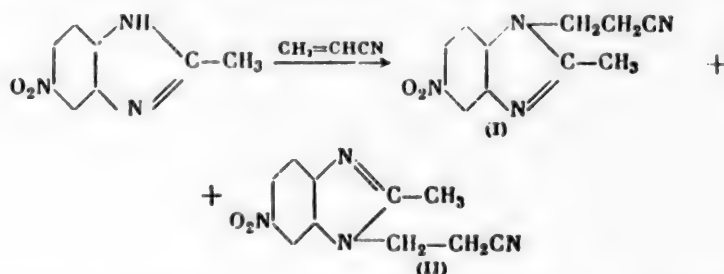
Leningrad Agricultural Institute

Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 11, pp. 3565-3569,

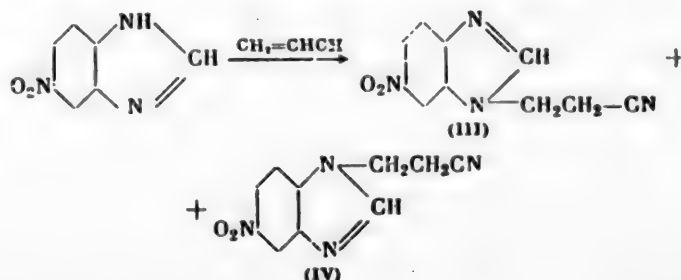
November, 1960

Original article submitted December 29, 1959

In a previous communication [1] reaction conditions for cyanoethylation of benzimidazolone and mercaptobenzimidazole were described. Continuing the investigation of new physiologically active substances in a series of nitrogenous heterocycles, we attempted in the present work the preparation of cyanoethylated derivatives of substituted benzimidazole, namely 5(6)-nitro- and 2-methyl-5(6)-nitrobenzimidazoles. On cyanoethylating 2-methyl-5(6)-nitrobenzimidazole two isomers are obtained: 1-cyanoethyl-2-methyl-5-nitrobenzimidazole with m. p. 205-206°C (I) and 1-cyanoethyl-2-methyl-6-nitrobenzimidazole with m. p. 191-192° (II).



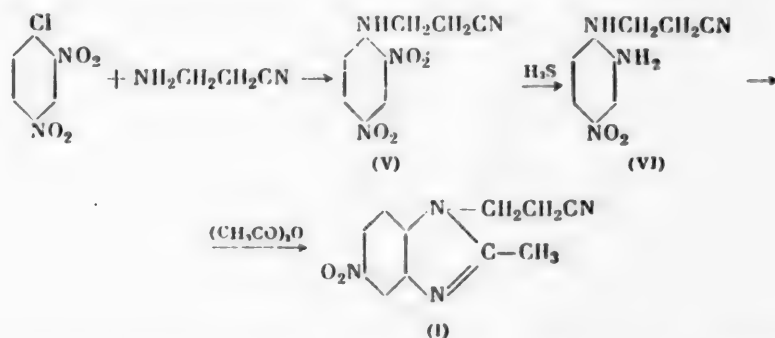
On cyanoethylating 5(6)-nitrobenzimidazole two isomers are obtained also: 1-cyanoethyl-6-nitrobenzimidazole with m. p. 187.5-189° (III) and 1-cyanoethyl-5-nitrobenzimidazole with m. p. 203-204° (IV).



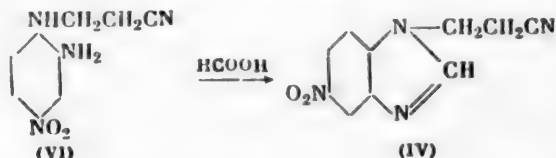
Bearing in mind that the basicity of isomers with a nitro group in the 6-position should be greater than the basicity of isomers with a nitro group in the 5-position owing to the effect of conjugation, it would be expected that the yield of 1-cyanoethyl-2-methyl-6-nitrobenzimidazole (II) and 1-cyanoethyl-6-nitrobenzimidazole (III) would be greater than the yield of the corresponding isomers with a nitro group in the 5-position, since cyanoethylation under similar conditions proceeds more readily the greater the basicity. In actual fact, the low-melting isomers (II) with m. p. 191-192° and (III) with m. p. 187.5-189° were obtained predominantly. Our observations are also confirmed by work on methylation of benzimidazole [2], in which it is established that the ratio of isomers obtained on methylating 5(6)-derivatives of benzimidazole depends on the properties of the substituent in the 5(6)-position, and especially on the pH of the reaction medium.

To determine the disposition of the nitro groups in the isomers obtained and to identify the latter we carried out counter synthesis of 1-cyanoethyl-2-methyl-5-nitrobenzimidazole (I) and 1-cyanoethyl-5-nitrobenzimidazole (IV). As the starting point in the synthesis we employed *β*-aminopropionitrile and 1-chloro-2,4-dinitrobenzene. The reaction proceeds exceedingly vigorously with evolution of heat, and is therefore carried out in a solvent at room temperature or with cooling. As a result, we obtained a good yield of 2,4-dinitro-*N*-*β*-cyanoethylaniline (V), a yellow crystalline product with m. p. 140-142°, from which by partial reduction of a nitro group with hydrogen in an alcoholic-ammoniacal medium was obtained 2-amino-4-nitro-*N*,*β*-cyanoethylaniline (VI), a red crystalline product with m. p. 167-168°.

By condensing (VI) with acetic anhydride a product with m. p. 205-206° was obtained, corresponding to isomer (I) in structure, i.e., to 1-cyanoethyl-2-methyl-5-nitrobenzimidazole.



A mixed sample of the two preparations gives no melting point depression. Consequently, the structure 1-cyanoethyl-2-methyl-6-nitrobenzimidazole corresponds to isomer (II) with m. p. 191-192°. On reacting (VI) with formic acid a product with m. p. 203-204° is obtained.

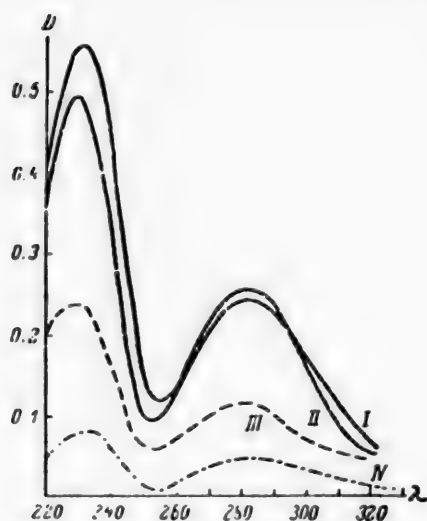


A sample of the product mixed with isomer (IV) does not give a melting depression. Accordingly, the structure 1-cyanoethyl-6-nitrobenzimidazole corresponds to isomer (III) with m. p. 187.5-189°.

To characterize the cyanoethylated substitution products of benzimidazole obtained (I-IV) we took ultraviolet absorption spectra in 1% aqueous hydrochloric acid solution on an SF-4 spectrophotometer in quartz cells with layer thickness 2 cm and with solution concentrations for substances (I) and (II)  $1 \cdot 10^{-5}$  and for substances (III) and (IV)  $1.2 \cdot 10^{-5}$  (see diagram).

#### EXPERIMENTAL

**Cyanoethylation of 2-methyl-5(6)-nitrobenzimidazole.** Into a round-bottomed flask fitted with reflux condenser, stirrer, dropping funnel, and thermometer were introduced 3.95 g of 2-methyl-5(6)-nitrobenzimidazole, 0.4 g of triethylbenzylammonium hydroxide, and 20 ml of dioxane. Three ml of acrylonitrile was added



Ultraviolet absorption spectra in 1% aqueous hydrochloric acid. I) 1-cyanoethyl-5-nitrobenzimidazole; II) 1-cyanoethyl-6-nitrobenzimidazole; III) 1-cyanoethyl-2-methyl-6-nitrobenzimidazole; IV) 1-cyanoethyl-2-methyl-5-nitrobenzimidazole.

dropwise to the solution with the temperature at 50-60°. As the acrylonitrile was poured in the reaction mixture resinified slightly and went into solution. On completion of the reaction, dioxane was distilled off in vacuo, and the crystalline residue dissolved in 75 ml of a 1-2% boiling hydrochloric acid solution with a pinch of animal charcoal. After cooling, the hydrochloric acid solution was treated with 8-10% ammonia until weakly alkaline. The precipitate settling out was filtered off, washed free of traces of ammonia with water, and dried at 105°. 4.96 g (95.2%) was obtained. The product was heated with 130 ml of water, a considerable amount of the crystals remaining undissolved. The residue insoluble in water was separated from the aqueous solution. 3.2 g (64.5%) of 1-cyanoethyl-2-methyl-6-nitrobenzimidazole (II) was obtained; it was readily soluble in acetone and in alcohol, and after recrystallizing from petroleum ether melted at 191-192°. A sample mixed with the starting material gave a sharp drop in melting point.

Found %: C 57.50; H 4.43; N 24.41.  $C_{11}H_{10}O_2N_4$ . Calculated %: C 57.39; H 4.34; N 24.34.

After distillation of water from the mother liquor in vacuo, 1-cyanoethyl-2-methyl-5-nitrobenzimidazole (I) was obtained as a white, crystalline substance, soluble in alcohol, toluene, and ethyl acetate. After recrystallization from alcohol it had m. p. 205-206°.

Found %: C 57.41; H 4.16; N 24.19.  $C_{11}H_{10}O_2N_4$ . Calculated %: C 57.39; H 4.34; N 24.34.

Cyanoethylation of 5(6)-nitrobenzimidazole was carried out similarly. To a mixture of 5 g of 5(6)-nitrobenzimidazole and 0.5 g of triethylbenzylammonium hydroxide in 20 ml of dioxane, 3.3 ml of acrylonitrile was added dropwise from a dropping funnel. The mixture was heated and stirred at 50-60° for 6-7 hours. On completion of the reaction the dioxane was distilled off in vacuo (15 mm), and the crystalline residue remaining dissolved in 100 ml of boiling 2% hydrochloric acid. After cooling the hydrochloric acid solution it was treated with 5-8% ammonia until it gave a weakly alkaline reaction. The precipitate of a mixture of isomers of 1-cyanoethyl-5(6)-nitrobenzimidazole separating out was washed with water and dried at 105°. To separate the isomers the precipitate was dissolved in 100 ml of boiling water. The precipitate insoluble in water was filtered off and dried at 105°. 4.8 g (80%) of 1-cyanoethyl-6-nitrobenzimidazole (III) was obtained; after recrystallizing from benzene a number of times and twice from acetoacetic ester, m. p. was 187.5-189°. It was a white substance, soluble in petroleum ether, alcohol, and acetone.

Found %: C 55.61, 55.73; H 3.7, 3.67; N 25.61, 25.77.  $C_{10}H_8O_2N_4$ . Calculated %: C 55.55; H 3.7; N 25.92.

After distilling off the aqueous mother liquor in vacuo, 1-cyanoethyl-5-nitrobenzimidazole (IV) was obtained. After drying at 105° and recrystallizing twice from alcohol and then from ethyl acetate, it had m. p. 203-204°, yield 1.1 g (18.3%).

Found %: C 55.48, 55.14; H 3.57, 3.74; N 25.60, 25.95.  $C_{10}H_8O_2N_4$ . Calculated %: C 55.55; H 3.7; N 25.92.

**2,4-Dinitro-N,β-cyanoethylaniline.** Into a round bottomed flask fitted with stirrer, reflux condenser, and thermometer was introduced 14.4 g of 2,4-dinitrochlorobenzene dissolved in 20 ml of dioxane. Five g of β-aminopropionitrile was gradually added dropwise with stirring and heating to 20-25°. After 2 hrs, brilliant yellow crystals of 2,4-dinitro-N,β-cyanoethylaniline began to settle out and were filtered off. Dioxane was removed in vacuo (15 mm). In all, 15.3 g (81.4%) of the substance was obtained. After one recrystallization from benzene and two from chloroform, m. p. was 141-142°, the substance forming brilliant yellow acicular crystals, soluble in ether and benzene.

Found %: C 45.87, 45.95; H 3.68, 3.87; N 23.76, 23.69.  $C_9H_8O_4N_4$ . Calculated %: C 45.75; H 3.34; N 23.73.

2-Amino-4-nitro-N,8-cyanoethylaniline. 2,4-Dinitro-N,8-cyanoethylaniline was subjected to partial reduction by hydrogen sulfide in an alcoholic - ammoniacal medium, similarly to the partial reduction of 2,4-dinitrobenzene [3]. 6.28 g of the substance was used in the reaction. Yield of 2-amino-4-nitro-N,8-cyanoethylaniline was 5 g (74.6%). Red, acicular crystals, readily soluble in alcohol, ether; m. p. 167-168° after recrystallizing from benzene.

Found %: C 52.22; H 4.74; N 26.97.  $C_9H_{10}O_2N_4$ . Calculated %: C 52.42; H 4.85; N 27.17.

Condensation of 2-amino-4-nitro-N,8-cyanoethylaniline with acetic anhydride. 1 g of the substance was placed in a 25 ml flask and freshly distilled acetic anhydride gradually added dropwise over a period of 1 hr. To the dark brown product 10 ml of 15% hydrochloric acid solution was added and the mixture heated for 1 hr. After cooling, the resulting solution was neutralized with ammonia until a weakly alkaline reaction was given. The 1-cyanoethyl-2-methyl-5-nitrobenzimidazole obtained was filtered off, washed with water, and dried out at 105°. The product was recrystallized twice from water with animal charcoal and from acetone. The white crystals obtained had m. p. 205-206°. A sample mixed with (I) gave no melting point depression.

Condensation of 2-amino-4-nitro-N,8-cyanoethylaniline with formic acid. A mixture of 1 g of 2-amino-4-nitro-N,8-cyanoethylaniline and 1.2 g of 90% formic acid (2.5 ml) was heated on a water bath for 2 hrs. After cooling, a 10% alkali solution was slowly added to the reaction mixture. The crude product was pressed out, washed with water, and purified a number of times by boiling in water with animal charcoal. After recrystallizing from benzene m. p. was 203-204°. A sample mixed with 1-cyanoethyl-5-nitrobenzimidazole (IV) gave no melting point depression.

#### SUMMARY

1. The cyanoethylation of 5(6)-nitrosubstituted benzimidazole was studied.
2. The following previously undescribed substances were prepared and characterized: 1-cyanoethyl-6-nitrobenzimidazole and 1-cyanoethyl-5-nitrobenzimidazole, 1-cyanoethyl-2-methyl-5-nitrobenzimidazole and 1-cyanoethyl-2-methyl-6-nitrobenzimidazole.
3. Ultraviolet absorption spectra of isomers of cyanoethylated benzimidazole derivatives were taken.

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# SYNTHESIS OF SEVERAL ACYL DERIVATIVES OF PHENOTHIAZINE

## III. DERIVATIVES OF NICOTINIC ACID

N. V. Khromov-Borisov, A. M. Yanovitskaya,  
and K. A. Eremicheva

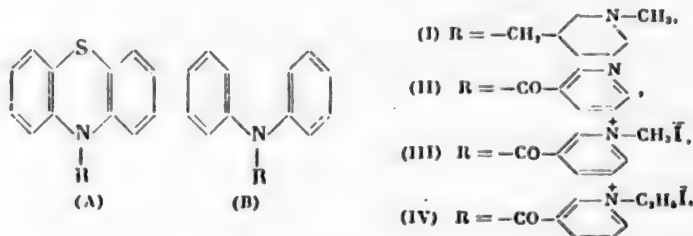
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Translated from *Zhurnal Obshchei Khimii*, Vol. 30, No. 11, pp. 3569-3572,

November, 1960

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Of the acyl derivatives of phenothiazine the derivatives of nicotinic acid have so far not been described. Several phenothiazine derivatives closely related structurally to its nicotinyl derivative appeared to be exceedingly valuable medical preparations.



Thus, 1-methylpiperidino-3-methyl-10-phenothiazine (A I), known by the name "pakatal," is of great interest as a medicinal preparation having a tranquilizing effect on the central nervous system, and close in its properties to aminazine [1].

While concerned with the synthesis of various phenothiazine derivatives [2], we synthesized in the present work nicotinyl-10-phenothiazine (A II), as well as its iodomethylate (A III) and iodoethylate (A IV). In the comparative study of the pharmacological properties of the compounds and with the aim of elucidating the relation between their chemical structure and biological activity we also synthesized similar diphenylamine derivatives: nicotinyl-diphenylamine (B II), its iodomethylate (B III) and iodoethylate (B IV). Preparation methods and properties of these compounds are described in the experimental section. The preparations synthesized were handed over for pharmacological investigation.

## EXPERIMENTAL

Hydrochloride of nicotinyl chloride [3]. 16 g of nicotinic acid was heated with 30 ml of thionyl chloride for 15 hrs in a flask fitted with a reflux condenser. The reaction product was quickly filtered off and dried in a vacuum desiccator. 24 g was obtained, m. p. 156°C. Yield was almost quantitative.

Hydrochloride of nicotinyl-10-phenothiazine. 6 g of phenothiazine in 150 ml of toluene was heated with 6 g of the hydrochloride of the acid chloride of nicotinic acid for 2.5 hrs under a reflux condenser. The

crystalline precipitate formed was filtered off, washed on the filter with toluene, and dried. After crystallizing twice from alcohol m. p. was 209-212°. 7.2 g (70.6%) was obtained. A bright green finely crystalline powder, readily soluble in warm alcohol and acetone. The salt hydrolyzed in aqueous solution.

Found %: N 8.47, 8.38; Cl 10.18, 10.32.  $C_{18}H_{13}ON_2SCl$ . Calculated %: N 8.22; Cl 10.42.

Nicotinyl-10-phenothiazine (base) (A II). 5 g of the hydrochloride of nicotinyl-10-phenothiazine was dissolved in 240 ml of alcohol. The solution was poured into 2 liters of dilute aqueous ammonia. The precipitate formed was filtered off, washed with water (until the ammoniacal odor disappeared), and dried. Recrystallized from alcohol the product had m. p. 111-112°. 3 g (70%) was obtained. A white amorphous powder, insoluble in water, readily soluble in organic solvents.

Found %: C 70.94, 70.16; H 4.16, 3.84; N 9.14, 9.09.  $C_{18}H_{12}ON_2S$ . Calculated %: C 71.05; H 3.94; N 9.21.

Iodomethylate of nicotinyl-10-phenothiazine (A III). 2 g of the base was dissolved in 20 ml of acetone. Excess methyl iodide (2.5 g) was added to the filtered solution. The reaction was carried out at room temperature. The precipitate settling out was filtered, washed on the filter with acetone, then with ether, and dried. Recrystallized from alcohol it had m. p. 231-233°. 2.6 g (90%) was obtained. A bright yellow crystalline powder, sparingly soluble in water, readily in hot alcohol.

Found %: N 6.38, 6.10; I 28.57, 28.63.  $C_{19}H_{15}ON_2SI$ . Calculated %: N 6.27; I 28.25.

Iodoethylate of nicotinyl-10-phenothiazine (A IV). 2 g of the base was dissolved in 50 ml of ethyl acetate. The solution was filtered and heated with excess ethyl iodide (2 ml) for 3 hrs. The solution then went from yellow-green to dark red. After removal of solvent the precipitate was treated with ether. We obtained 1.6 g of substance, m. p. 225-228° (without crystallizing). After crystallizing from alcohol, 1 g (33.3%) of substance was obtained with m. p. 228-230°. The substance formed yellow-orange crystals. Solubility in water at 18° was 0.15-0.2%, at 30-40° about 0.4%; in alcohol it was about 5% at room temperature.

Found %: N 6.16, 6.13; I 27.36, 27.79.  $C_{20}H_{17}ON_2SI$ . Calculated %: N 6.08; I 27.60.

Hydrochloride of N-nicotinyldiphenylamine. 3.4 g of diphenylamine was dissolved in 100 ml of toluene. 4 g of the hydrochloride of the acid chloride of nicotinic acid was added to the solution. The mixture was heated for 3 hrs under a reflux condenser. The reaction was accompanied by evolution of hydrogen chloride. A copious precipitate was formed during the reaction process and was filtered off and dried. The product, recrystallized from alcohol, had m. p. 214-215°. 5.5 g (89%) was obtained. A light-yellow (with a grayish tinge) powder, readily soluble in water and alcohol, insoluble in ether. After standing for a short while, aqueous solutions hydrolyzed.

Found %: N 9.13, 9.42; Cl 11.45, 11.78.  $C_{18}H_{15}ON_2Cl$ . Calculated %: N 9.01; Cl 11.43.

N-Nicotinyldiphenylamine (base) (B II). 3 g of the hydrochloride of N-nicotinyldiphenylamine was dissolved in 50 ml of water; the solution was filtered and slowly added to 500 ml of water made strongly alkaline with soda. The precipitate formed was filtered off, washed with water and dried. 1.8 g (90%) was obtained, m. p. 147-148° (from alcohol).

Found %: C 78.64, 78.99; H 5.34, 5.20; N 10.54, 10.41.  $C_{18}H_{14}ON_2$ . Calculated %: C 78.83; H 5.15; N 10.22.

Iodomethylate of N-nicotinyldiphenylamine (B III). 0.82 g of N-nicotinyldiphenylamine (base) was dissolved in 10 ml of acetone. Excess methyl iodide (1 ml) was added to the solution at room temperature. After several hours a precipitate separated out. 0.9 g (75%) of a substance was obtained, m. p. 217-219° (without crystallizing). Crystallizing from alcohol gave no change in melting point. The substance formed a pale-yellow crystalline powder, sparingly soluble in water and alcohol at room temperature (0.20-0.25%), readily soluble in hot alcohol.

Found %: I 31.00, 30.63.  $C_{19}H_{17}ON_2I$ . Calculated %: I 30.53.

Iodoethylate of N-nicotinyldiphenylamine (B IV). 0.82 g of the base N-nicotinyldiphenylamine was dissolved in 10 ml of ethyl acetate. The solution was filtered and heated for 2.5 hrs with excess ethyl iodide. After solvent removal (at room temperature) the remaining resinous product was treated with ether (with prolonged grinding). 0.95 g of raw material was isolated. After crystallizing from alcohol 0.69 g (53%) of a

substance with m. p. 139-141° was obtained. It formed a yellow crystalline powder with a grayish tinge, sparingly soluble in water (0.20-0.25%), more readily so in alcohol.

Found %: I 29.40, 29.36.  $C_{20}H_{19}ON_2I$ . Calculated %: I 29.53.

#### SUMMARY

1. Nicotiny1-10-phenothiazine, its hydrochloride, iodomethylate, and iodoethylate were synthesized.
2. Analogs of these compounds were prepared containing no sulfur in the molecule, namely, N-nicotinyldiphenylamine, its hydrochloride, iodomethylate, and iodoethylate.

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## THE CHEMISTRY OF ONIUM COMPOUNDS

### III. A STUDY OF THE THERMAL DECOMPOSITION OF REACTION PRODUCTS OF TETRAHYDROFURAN, $\alpha$ -METHYLFURAN, PYRROLE, AND THIOPHENE WITH MAGNESIUM IODIDE DIETHERATE AND WITH MAGNESIUM IODIDE

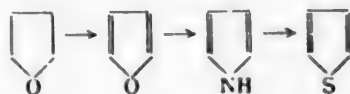
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November, 1960

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One of us has previously shown that aliphatic ethers with bulkier radicals than ethyl [1] and, more readily, dioxane [2] equimolecularly displace diethyl ether from  $\text{MgI}_2 \cdot 2 (\text{C}_2\text{H}_5)_2\text{O}$  and form with  $\text{MgI}_2$  oxonium salts with a more stable magnesium to oxygen bond than the one in the molecules of the substituted ethereal compound. During this investigation we undertook the study of the reaction of five-membered heterocyclic compounds, in the first place with  $\text{MgI}_2 \cdot 2(\text{C}_2\text{H}_5)_2\text{O}$ . In this regard, it was established that tetrahydrofuran enters into exothermic reactions with magnesium iodide dietherate and equimolecularly displaces diethyl ether from it; on the other hand,  $\alpha$ -methylfuran reacted with magnesium iodide dietherate at an appreciable rate only above  $70^\circ\text{C}$  and on subsequent heating to  $100^\circ$  displaced from it one less stably bound diethyl ether molecule. The reaction of pyrrole with magnesium iodide dietherate proceeds with still greater difficulty, a molecule of ethyl ether being displaced only at about  $135^\circ$ . Thiophene does not react completely with magnesium iodide dietherate even on prolonged heating at  $85$ - $90^\circ$ . Thus, magnesium iodide dietherate appeared to be a convenient yardstick in the comparative estimation of the degree of aromaticity of five-membered O-, N-, and S-heterocyclic compounds, the elucidation of which was first undertaken by Bamberger [3], and later interpreted from the viewpoint of the electronic theory by Robinson [4]. The heterocyclic compounds enumerated can be arranged in the order



with regard to increase in reluctance to giving up an unshared electron pair from the heteroatoms with formation of "onium bonds," and in the case of sylvan, pyrrole, and thiophene, with regard to increase in stability of the electron sextet of the heteronucleus.

This order is also confirmed by data gained in the study of the thermal decomposition of reaction products of the heterocyclic compounds indicated, with anhydrous magnesium iodide. Tetrahydrofuran forms with the latter a compound decomposing on heating, with disruption of the heterocycle [5]. Sylvan and pyrrole only on heating give with magnesium iodide compounds decomposing at high temperatures also with disruption of the heterocycles. Thiophene does not react with magnesium iodide even on prolonged heating. From this it follows that furan and pyrrole and their compounds retain a "benzoid type" state of the electrons in the heteronuclei only at low temperatures; with increase in temperature the nucleus is disrupted, unshared pairs of oxygen and nitrogen electrons being liberated, thereby allowing the formation of stable onium bonds with magnesium subiodide.



this also explains the decomposition of O- and N-heteronuclei on heating similar compounds. The course of the decomposition of sylvan and pyrrole compounds with  $\text{MgI}_2$ , together with the above, forces the conclusion that, besides formation of onium salts, condensation reactions of sylvan and pyrrole occur at elevated temperatures.

The ability of the indicated heterocyclic compounds to form onium salts can hardly be proposed as being related to the polarity of their molecules. Thus, in the aliphatic ether series, with increase in mass the dipole moments of the radicals entering them decrease:  $\text{CH}_3-\text{O}-\text{CH}_3$ , 1.29D;  $\text{C}_2\text{H}_5-\text{O}-\text{C}_2\text{H}_5$ , 1.12D;  $\text{Iso}-(\text{C}_5\text{H}_{11})_2\text{O}$ , 1.0D [6]. The last ether displaces diethyl ether from  $\text{MgI}_2 \cdot 2(\text{C}_2\text{H}_5)_2\text{O}$  [1]. Considering, too, the fact that dioxane with a dipole moment of the order of 0.4 D [7] acts on  $\text{MgI}_2 \cdot 2(\text{C}_2\text{H}_5)_2\text{O}$  still more vigorously, the conclusion must be made that in substances of ether type the ability to form onium compounds increases with decrease in polarity of their molecules. However, sylvan\* does not displace diethyl ether from  $\text{MgI}_2 \cdot 2(\text{C}_2\text{H}_5)_2\text{O}$  under ordinary conditions; on the contrary, tetrahydrofuran with dipole moment 1.81 D [8] readily displaces it.

A definite relationship between the above ability and magnitudes of the angles between valences in the heteroatoms was not observed either. In the ether series, with increase in molecular weight and decrease in polarity the angle between the valences at the oxygen must increase from the limiting value of  $111^\circ$  in  $\text{CH}_3-\text{O}-\text{CH}_3$  [9]. On the one hand, diisopropyl ether, with a greater valence angle at the oxygen, and on the other hand, dioxane with a corresponding angle of  $110^\circ$  [10], smaller than the angle between the oxygen valences in diethyl ether, displace the latter from  $\text{MgI}_2 \cdot 2(\text{C}_2\text{H}_5)_2\text{O}$ . Almost the reverse effect is observed in O-heterocyclic compounds: Tetrahydrofuran with a valence angle of  $111 \pm 2^\circ$  [11] displaces diethyl ether from  $\text{MgI}_2 \cdot 2(\text{C}_2\text{H}_5)_2\text{O}$ , but sylvan, with a smaller valence angle,\*\* does not displace it. Thus, the ability of heteroatoms to form onium bonds is not limited by any one property of the molecules containing them or of the heteroatom itself. A clue to the solution of this question may be sought in the specificity of the mutual influences of the atoms found in the heterocycles, since the participation of heteroatoms in formation of cyclic systems increases their ability to form onium compounds. By way of confirmation of the proposition can be quoted the fact established by us that dioxane and tetrahydrofuran form with  $\text{MgI}_2$  stabler compounds than do aliphatic ethers.

## EXPERIMENTAL

Experiments performed in the study of the thermal decomposition of products of the reaction of chemically pure heterocyclic compounds with magnesium iodide dietherate and with magnesium iodide were carried out in the apparatus described previously [1]. The  $\text{MgI}_2$  was prepared by thermal decomposition of magnesium iodide dietherate.

### 1. Experiments with Tetrahydrofuran\*\*\*

a) Mixing 0.1 mole of melted  $\text{MgI}_2 \cdot 2(\text{C}_2\text{H}_5)_2\text{O}$  with 0.1 mole of tetrahydrofuran was accompanied by heating and elimination of liquid by evaporation. On heating further to  $100^\circ$  until evaporation ceased completely, 7 g of a liquid was obtained with b. p.  $35-36^\circ$  (753 mm), completely soluble in concentrated hydrochloric acid. Mixing of the reaction product cooled to  $20^\circ$  with 0.1 mole of tetrahydrofuran also proceeded with evaporation of a liquid from which, after heating to  $100^\circ$ , 6.8 g of diethyl ether was obtained with b. p.  $35-36^\circ$  (753 mm). Thus, tetrahydrofuranequimolecularly displaces diethyl ether from  $\text{MgI}_2 \cdot 2(\text{C}_2\text{H}_5)_2\text{O}$ . After heating for 3 hrs at  $225-230^\circ$  and for 2 hrs at  $350-360^\circ$ , from  $\text{MgI}_2 \cdot 2\text{C}_4\text{H}_8\text{O}$ , 12 g and 2 g respectively of dark-colored liquid distillates and 1.35 liters of a gas ( $24^\circ$ , 747 mm) were obtained. In the gas were found 1.75% hydrogen, 0.5% saturated and 7.2% unsaturated hydrocarbons. From the liquid distillate were isolated 4.4 g of tetrahydrofuran with b. p.  $63.5-64^\circ$  (749 mm),  $d_4^{20}$  0.8930,  $n_D^{20}$  1.4025; and 3 g of a fraction with b. p.  $66-85^\circ$ . The residue from fractionation contained 6 g of iodine.

b) Reaction of 0.1 mole of  $\text{MgI}_2$  with 0.2 mole of tetrahydrofuran proceeded exothermally with formation of a white, voluminous substance. After heating for 3 hrs at  $135-150^\circ$  and  $195-200^\circ$ , 6.8 g of liquid distillate

\* The dipole moment for furan is known - 0.7 D [8].

\*\* Valence angle at the oxygen in furan is equal to  $107 \pm 3^\circ$  [11].

\*\*\* We express our thanks to G. I. Kuznetsova for presenting the tetrahydrofuran.

was obtained from it, containing 5.6 g of tetrahydrofuran with b. p. 63-64° (744 mm),  $d_4^{20}$  0.8960. On decomposing the product further at 360°, 1.5 liters of a gas was obtained (22°, 748 mm) in which were found 2.1% of hydrogen, 0.68% of saturated and 6.6% of unsaturated hydrocarbons, and 7 g of a dark-colored liquid. From the latter were isolated 1.0 g of tetrahydrofuran and 1.3 g of a fraction with b. p. 66-85°. The residue from the fractionation contained 4.4 g of iodine. Thus, of the two molecules of tetrahydrofuran combined with  $MgI_2$ , only one underwent fission.

## 2. Experiments with Sylvan\*

a) Addition of 0.2 mole of sylvan to 0.1 mole of  $MgI_2 \cdot 2(C_2H_5)_2O$  did not result in any temperature change. After heating for 3 hrs at 100°, 14.1 g of liquid distillate was obtained, from which were isolated 6.9 g of diethyl ether and 6.5 g of sylvan. From these data it follows that only at an elevated temperature is sylvan capable of displacing one molecule of diethyl ether from  $MgI_2 \cdot 2(C_2H_5)_2O$ . After heating for 3 hrs at 170-200°, with subsequent heating to 360°, 0.55 liter of a gas (22°, 740 mm) and 18.3 g of liquid distillate were obtained. On fractionating the latter the following were isolated: 3 g of diethyl ether with b. p. 35-36°, 7.8 g of sylvan with b. p. 63-63.5° (750 mm),  $d_4^{20}$  0.9100,  $n_D^{20}$  1.4290, and 4 g of ethyl iodide with b. p. 71-72°,  $d_4^{20}$  1.9271,  $n_D^{20}$  1.5100. In the residue from the distillation was found 3 g of iodine. Decomposition was accompanied also by HI formation. Formation of ethyl iodide is connected with the action of HI on the complex product containing diethyl ether [1]. Sylvan underwent rupture only to a slight degree.

b) On heating a mixture of 0.1 mole of  $MgI_2$  and 0.2 mole of sylvan, a dark, viscous product was formed. At 170° an exothermic reaction began, with increase in temperature to 180°. After heating for 3 hrs at 195-200°, 3.5 g of a liquid distillate was obtained, including 2.6 g of sylvan with b. p. 63-64° (749). On further heating to 360°, 0.6 liter of a gas (20°, 749 mm) was obtained, containing 5.8% hydrogen, 0.2% saturated and 1.65% unsaturated hydrocarbons, and 3.5 g of liquid distillate, in which was found 2.7 g of iodine. Decomposition was accompanied by HI formation and sublimation of iodine.

## 3. Experiments with Pyrrole

a) After mixing 0.1 mole of  $MgI_2 \cdot 2(C_2H_5)_2O$  and 0.2 mole of pyrrole and heating to 135-138°, a liquid began to evaporate off. From 7.3 g of distillate, 6.8 g of diethyl ether with b. p. 35-36° was obtained, completely soluble in concentrated hydrochloric acid. Thus, under the given conditions, the following reaction proceeded:  $MgI_2 \cdot 2(C_2H_5)_2O + 2C_4H_5N \rightarrow MgI_2 \cdot (C_2H_5)_2O \cdot 2C_4H_5N + (C_2H_5)_2O$ . On heating the latter product to 360°, 8.2 g of a liquid distillate was obtained, from which were isolated 3.4 g of diethyl ether and 4 g of pyrrole, with b. p. 128-129° (747 mm),  $d_4^{20}$  0.9740,  $n_D^{20}$  1.5080. The carbonlike residue from the decomposition was treated with caustic soda solution and then with steam. 0.3913 g of ammonia was found in the distillate (150 ml).

b) On heating a mixture of 0.1 mole of  $MgI_2$  and 0.2 mole of pyrrole to 134-135°, an exothermic reaction began, the temperature rising to 145-147°, and a dark, viscous product being formed. After heating for 2 hrs at 150°, 0.9 g of pyrrole was distilled off from it. It was then treated four times with 10 ml of water with subsequent distillations of a liquid. From 36 g of the liquid distillate, 5 g of pyrrole was isolated with b. p. 128-128.5° (747 mm),  $d_4^{20}$  0.9750. In this way it was shown that one of the pyrrole molecules is more stably bound to the  $MgI_2$ . After treatment with water, the product was subjected to decomposition at a temperature of 360°. About 5 ml of a liquid was obtained, from which was isolated 0.9 g of pyrrole. After alkalization, the dry residue in the flask was treated with steam, 0.2540 g of ammonia being found in the distillate (150 ml).

## 4. Experiments with Thiophene\*

a) After addition of 0.2 mole of thiophene to 0.1 mole of  $MgI_2 \cdot 2(C_2H_5)_2O$  and subsequent heating, first at 85-90° and then at 125-130°, 17.6 g of a liquid distillate was obtained, from which was isolated 15.9 g of thiophene with b. p. 83.5-84° (753 mm),  $d_4^{20}$  1.0641,  $n_D^{20}$  1.5288.

b) After addition of 0.2 mole of thiophene to 0.1 mole of  $MgI_2$  and subsequent heating for 2 hrs at 100°, 16.5 g of a liquid distillate was obtained, giving on fractionation 16.3 g of thiophene with b. p. 84° (753 mm).

\* We express our thanks to L. F. Bel'skii for presenting the sylvan.

\*\* We express our thanks to S. Z. Talts for presentation of thiophene.



## SUMMARY

1. It was shown that tetrahydrofuran equimolecularly displaces diethyl ether from  $\text{MgI}_2 \cdot 2(\text{C}_2\text{H}_5)_2\text{O}$  and gives the compound  $\text{MgI}_2 \cdot 2\text{C}_4\text{H}_8\text{O}$ , the decomposition of which proceeds with decomposition of one molecule of tetrahydrofuran.
2. It was established that sylvan and pyrrole on heating displace one molecule of diethyl ether from  $\text{MgI}_2 \cdot 2(\text{C}_2\text{H}_5)_2\text{O}$ , and with  $\text{MgI}_2$  form compounds decomposing with heterocycle disruption.
3. It was shown that thiophene reacts neither with  $\text{MgI}_2 \cdot 2(\text{C}_2\text{H}_5)_2\text{O}$  nor with  $\text{MgI}_2$ .
4. The proposition was put forward that participation of heteroatoms in formation of heterocyclic nuclei increases their ability to formonium compounds.

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## 2-MERCAPTOBENZOTHAZOLE IN THE MANNICH REACTION

### II. THE REACTION OF N-CHLOROMETHYLBENZOTHAZOLETHIONE-2 WITH AMINES

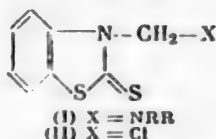
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Institute of Medical Parasitology and Tropical Medicine

Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 11, pp. 3576-3578,  
November, 1960

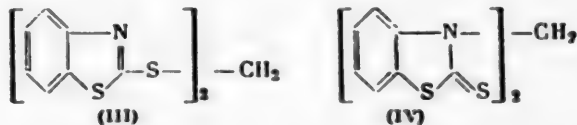
Original article submitted November 23, 1959

In a previous work [1] we undertook the elucidation of the structure of the Mannich bases of 2-mercaptobenzothiazole (I, X = NRR) by synthesizing them from N-hydroxymethylbenzothiazolethione-2 with parallel conversion of the latter into N-chloromethylbenzothiazolethione-2 (II, X = Cl) and then into N-methylbenzothiazolethione-2.



The product corresponded entirely to the N-methyl derivative of the thione form of 2-mercaptobenzothiazole described in the literature.

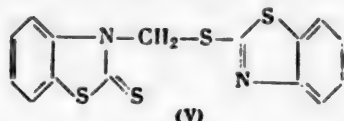
We conjectured that reacting (II) with the amines used previously by us in a Mannich reaction could be another method of synthesizing the Mannich bases indicated, and also be confirmation of their thione structure. In an attempt to carry out condensation of (II) with piperidine and morpholine at room temperature or with short heating, the hydrochloride of the corresponding amine was obtained in almost theoretical yield. Also, formation of the identical substance with m. p. 132°C was observed in all experiments. Investigation of this compound showed that it was comparatively resistant to the action of dilute alkalis and hydrochloric acid. According to the analytical data the substance was evidently bis-(mercaptobenzothiazolyl)-methane, but in its melting point it differed from derivatives of this type described in the literature [2]: bis-(S-benzothiazolyl-mercapto)-methane (III) and bis-(N-benzothiazolylthione)-methane (IV).



It was probable that in our case a compound was formed in which a methylene group was bound to the cyclic nitrogen atom of one benzothiazole residue and to the exocyclic sulfur atom of the other. Measurement of the UV spectrum of this compound and comparison of curve 3 obtained with the absorption curves of N-methylbenzothiazolethione-2 (1) and S-methylmercaptobenzothiazole (2)\* showed the presence in it of thione and thiol structures (see diagram). To confirm the above proposition, condensation of (II) with the Na salt of

\* The dipole moment for furan is known - 0.7 D [8].

2-mercaptobenzothiazole was carried out. The reaction product appeared identical with the substance obtained in every case of the reaction of (II) with amines. Further proof of the structure of the compound obtained was afforded by its isomerization into (IV) on heating in the presence of iodine (compare the conversion of (III) into (IV) [2]). The data obtained permitted us to ascribe to the substance the structure (N-benzothiazolylthione)-(S-benzothiazolylmercapto)-methane (V), previously undescribed in literature.



Proceeding from the assumption that the basicity of the amine will influence the similar reaction course of (II) with piperidine and morpholine, the amine was substituted by an equimolecular quantity of caustic potash. Conducting the reaction both at room temperature and at the boiling point of alcohol led to the formation of substance (V) in 64-65% yield. Besides this product, a substance was isolated with m. p. 247-248°, its identification not being attempted.

## EXPERIMENTAL

### Reaction of N-Chloromethylbenzothiazolethione-2 (II) with Amines

a) With piperidine. 5.4 g (0.025 mole) of (II) was mixed with 4.3 g (0.05 mole) of piperidine; the mixture was heated to 80°, when it solidified. The product was mixed with 50 ml of benzene, heated for a short time under a reflux condenser, and filtered hot; weight of residue was 3.3 g, m. p. 235°, giving no depression with piperidine hydrochloride. On cooling, a pale crystalline substance with m. p. 125° separated from the filtrate. After crystallizing from ethyl acetate and then from a mixture of toluene and petroleum ether (1:1), 3.0 g, m. p. 132-132.5°, was obtained. Colorless needles, readily soluble in benzene, toluene, ethyl acetate, alcohol, less so in petroleum ether, insoluble in water.

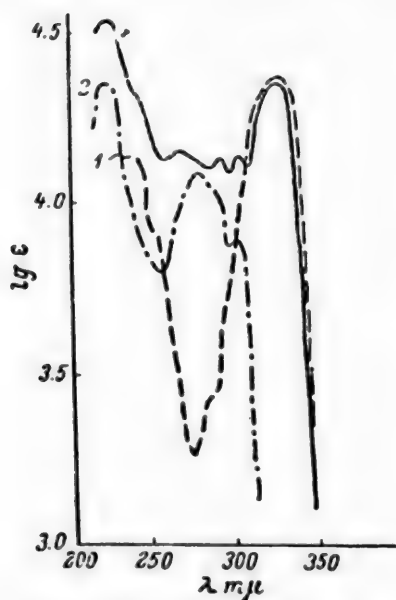
$\lambda_{\max}$  (alcohol) 224, 265, 289, 299, 325 m $\mu$  (log  $\epsilon$  4.527, 4.140, 4.108, 4.130, 4.334). Found %: C 51.81, 51.88; H 3.24, 3.22; N 8.20, 8.20. M 331.  $C_{15}H_{10}N_2S_4$ . Calculated %: C 52.02; H 2.89; N 8.09, M 346.

The substance did not form a precipitate with silver nitrate, did not undergo any change on reacting with alcoholic hydrochloric acid, or on heating with alcoholic ammonia solution, 10% hydrochloric acid or 10% caustic soda.

b) With morpholine. To a solution of 1.8 g (0.0085 mole) of (II) in 20 ml of benzene at 40°, 1.55 g (0.017 mole) of morpholine was added. After several hours a precipitate began to separate out. On the following day 0.85 g of morpholine hydrochloride was filtered off. On cooling, a crystalline precipitate separated out from the solution when concentrated, m. p. 131-132° [from ethyl acetate and from a mixture of benzene and petroleum ether (1:1)]; yield 1.15 g (79.5%). The substance did not give a melting point depression when mixed with a sample obtained from experiment "a."

### Reaction of (II) with Alkali

a) A solution of 9.3 g (0.043 mole) of (II) in 200 ml of anhydrous alcohol and 50 ml of anhydrous benzene containing 2.4 g (0.043 mole) of caustic potash were stirred for 40 hrs at room temperature. The colorless precipitate settling out was filtered off (8.7 g, pH of filtrate 6), washed with water until the wash water was free of chlorine ions; after drying, it weighed 5.6 g, m. p. 125-200°. Concentration of the alcohol-benzene filtrate by evaporation gave an oily residue.



Ultraviolet absorption spectra. 1) N-Methylbenzothiazolethione-2; 2) S-methylmercaptobenzothiazole; 3) the compound synthesized.

On grinding this with ethyl acetate 1.0 g of a substance with m. p. 125 - 190° was obtained. Crystallization of the combined portions (6.6 g) from benzene gave 4.9 g (65.4%) of (V) and 1.6 g of a compound with m. p. 247-248° (from toluene).

b) From 5.35 g (0.025 mole) of (II), on boiling for 40 minutes with 9 ml of an alcoholic solution containing 0.025 mole of caustic potash, 2.75 g (64%) of (V) and 0.70 g of a substance with m. p. 244-246° were obtained.

(N-Benzothiazolythione) - (S-benzothiazolylmercapto)-methane (V)

To 75 ml of anhydrous alcohol containing 0.01 g-at. of sodium, 1.67 g (0.01 mole) of 2-mercaptobenzothiazole was added at 32°; the solution was cooled to 18° and 2.15 g (0.01 mole) of (II) introduced into it. After 30 minutes the resulting suspension was heated to boiling and held at this temperature for 30 minutes. The precipitate settling out was filtered off (pH of filtrate 8.6), washed with water and dissolved in 100 ml of benzene. The solvent was evaporated from the dried extract and the residue crystallized from ethyl acetate; yield of (V) was 3.0 g (87%), m. p. 131-132°, giving no melting point depression when a sample was mixed with the product of the reaction of (II) with piperidine, morpholine, or alkali.

Isomerization of (V) into (IV). 0.85 g (0.0025 mole) of (V) and a small crystal of iodine were heated on an oil bath for 2.5 hrs at 200-230°. The solid product was pulverized, washed with methyl alcohol, and crystallized from pyridine. Yield of (IV) was quantitative, m. p. 292-293° (corresponding with the literature [2]).

SUMMARY

The reaction was achieved of N-chloromethylbenzothiazolethione-2 with piperidine, morpholine, and alkali, and the reaction product identified as (N-benzothiazolythione)-(S-benzothiazolylmercapto)-methane.

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# THE REACTION OF CHROMONECARBOXYLIC-2 ACIDS AND THEIR ESTERS WITH DIAMINES

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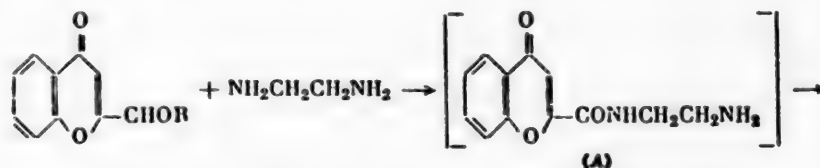
Original article submitted December 23, 1959

It is known that the  $\gamma$ -pyrone ring of chromones is ruptured quite readily by bases, including aliphatic amines. 2-B-Benzylaminocrotonoylphenol is obtained by the action of benzylamine on 2-methylchromone [1]. With hydrazine the simplest chromones usually form 3-o-hydroxyphenylpyrazoles [1-3], and not hydrazones, as assumed previously [4]. The methyl and ethyl esters of chromonecarboxylic-2 acid with excess hydrazine hydrate give the hydrazide of 3-(2'-hydroxyphenyl)-pyrazolecarboxylic-5 acid [5]. With equimolecular quantities of hydrazine hydrate these esters are converted, in the author's opinion [5], into a pyrazolidone derivative by addition of one hydrazine amino group at the double bond of the  $\gamma$ -pyrone ring and subsequent intramolecular amidation of the other amino group of the carbalkoxyl residue.

In the present work it is established that chromonecarboxylic-2 acids are readily reclosed in the corresponding 3-(2'-hydroxyphenyl)-pyrazolecarboxylic-5 acids by the action of hydrazine hydrate. We synthesized by the method indicated a series of representatives of this class (Table 1). Acids (I-VII) can be obtained in aqueous solution as their salts.

Continuing the study of the properties of derivatives of chromonecarboxylic-2 acid [6, 7], we investigated the nature of the reaction of esters of this acid with ethylenediamine. As expected, the reaction is complicated, a series of substances of neutral and basic character being formed. Nevertheless, in the case of the esters of unsubstituted chromonecarboxylic-2 acid we succeeded in preparing the desired 3-(2'-hydroxybenzoylmethylene)-piperazinone-2 (VIII) in 40-48% yield.

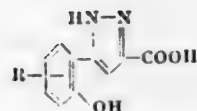
Somewhat earlier, Polish authors [8], during a study of the reaction of the ethyl ester of chromonecarboxylic-2 acid with ethylenediamine (experimental conditions not indicated), isolated, besides other substances, a substance of composition  $C_{12}H_{12}O_3N_2$  with m. p. 213-214.5°C (yield 10%), which was undoubtedly identical with piperazinone (VIII). Piperazinone (VIII) is very likely formed from intermediate  $\beta$ -aminoethylamide (A) by intramolecular aminolysis of the pyrone ring, this being confirmed by observations [8] on the more rapid course of amidation of the ester of chromonecarboxylic-2 acid by primary amines in comparison with rupture of the pyrone ring.\*



\*The authors [8] in their brief communication do not deal with the question of the detailed structure of compound (VIII). Their ideas on the course of the formation of this compound coincide with ours.

TABLE 1

3-(2'-Hydroxyphenyl)-pyrazolecarboxylic-5 Acids

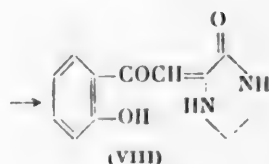


Sub- stance No.	Substituents in original chromone- carboxylic-2 acids	R	Molecular formula	Yield, %	Melting point*	% N	
						found	calcd.
(I)	—	H	C <sub>10</sub> H <sub>8</sub> O <sub>3</sub> N <sub>2</sub> **	85.5	234–235°	—	—
(II)	6-CH <sub>3</sub>	5'-CH <sub>3</sub>	C <sub>11</sub> H <sub>10</sub> O <sub>3</sub> N <sub>2</sub>	83.5	277°	12.83	12.84
(III)	7-CH <sub>3</sub>	4'-CH <sub>3</sub>	C <sub>11</sub> H <sub>10</sub> O <sub>3</sub> N <sub>2</sub>	97.3	283°	12.66	12.84
(IV)	6-Cl	5'-Cl	C <sub>10</sub> H <sub>7</sub> O <sub>3</sub> N <sub>2</sub> Cl	75.6	307°	12.02	11.74
(V)	7-CH <sub>3</sub> O	4'-CH <sub>3</sub> O	C <sub>11</sub> H <sub>10</sub> O <sub>4</sub> N <sub>2</sub>	95.7	251–252°	11.92	11.96
(VI)	6-NO <sub>2</sub>	5'-NO <sub>2</sub>	C <sub>10</sub> H <sub>7</sub> O <sub>5</sub> N <sub>3</sub>	83.3	226–228°	17.03	16.86
(VII)	6,8-Br	4',5'-Br	C <sub>10</sub> H <sub>6</sub> O <sub>3</sub> N <sub>2</sub> Br <sub>2</sub> ***	82.9	314°	7.52	7.74

\* Acids (II–IV, VI, VII) decompose on melting. Acids (II and VII) were recrystallized from alcohol, the remainder from dilute alcohol.

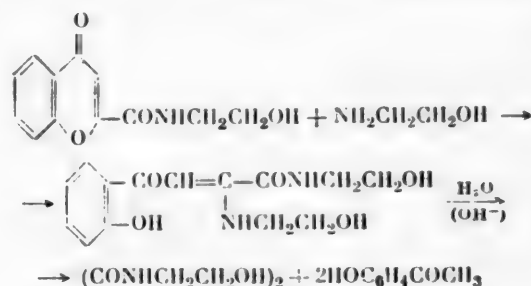
\*\* Found %: C 58.76; H 4.19. Calculated %: C 58.81; H 3.95.

\*\*\* Found %: Br 44.60. Calculated %: Br 44.15.



By-products in the reaction can arise from the reaction of aminoethylamide (A) with another ester molecule [a high-melting, difficultly soluble substance was obtained, probably N,N'-dichromonoyl-(2)-ethylenediamine], and also as a result of opening of the pyrone ring by ethylenediamine before onset of amidation.

We encountered extensive rupture of the  $\gamma$ -pyrone system on treatment of the ethyl ester of chromone-carboxylic-2 acid with aminoethanol in alcohol (boiling for 2 hrs). The originally formed  $\beta$ -hydroxyethylamide of chromonecarboxylic-2 acid [8], which is also obtained from the acid chloride of this acid [7], when reacted with excess aminoethanol gave as one of the reaction products the already known di-( $\beta$ -hydroxyethylamide) of oxalic acid, m. p. 166.5–167°. The scheme of the rupture can be represented thus.



It is quite worthy of note that it is not possible to obtain piperazinone (VIII) from ethylenediamine and the ester of *o*-hydroxybenzoylpyrrolacetic acid. In contrast to this, closing of the nitrogen (pyrazole) ring under the influence of hydrazine hydrate can be achieved if we proceed either from chromones or from the diketones preceding them (in the syntheses) [5].

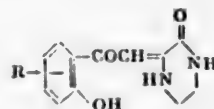


To ascertain the factors influencing the relative yields of piperazinone (VIII) and other reaction products, reaction conditions were varied: ratio of reagents and their concentration; nature of solvent (alcohol or benzene); temperature; order of addition of reagents. With a large excess of ethylenediamine in the absence of solvent ( $\sim 100^\circ$ , 1.5 hrs) piperazinone (VIII) is not obtained, probably because of the intense rupture of the 2-carbomethoxychromone molecule then proceeding. Decrease in concentration of the initial reagents, which should promote the process of intramolecular cyclization, results in complete disappearance of the high-melting by-product. The other factors mentioned above have little influence.

Substitution of the ethyl ester of chromonecarboxylic-2 acid by the methyl or phenyl one does not lead to substantial alteration in yield of piperazinone (VIII). Introduction of substituents into the benzene nucleus of esters of the chromonecarboxylic acid has a small but nevertheless noticeable influence on the character of the reaction of the esters with ethylenediamine. Presence of a halogen or nitro group in the 6-position in the ester causes somewhat increased yields (56-63% of sufficiently pure products) of the corresponding piperazinones (see Table 2). On the other hand, the presence of electron-donating substituents ( $\text{CH}_3$ ,  $\text{CH}_3\text{O}$ ) has an adverse effect on yield of piperazinones (22-23% of pure and no greater than 37% of crude reaction products).

TABLE 2

3-(2'-Hydroxybenzoylmethylene)-piperazinones-2



Compound No.	Substituents in initial esters of chromonecarboxylic-2 acid <sup>a</sup>	R	Molecular formula	Yield (%) <sup>b</sup>	Melting point <sup>c</sup>	% N:	
						found	calcd.
(VIII)	—	H	$\text{C}_{12}\text{H}_{12}\text{O}_3\text{N}_2$	48	218–219°	11.93d	12.06
(IX)	6- $\text{CH}_3$	5'- $\text{CH}_3$	$\text{C}_{13}\text{H}_{14}\text{O}_3\text{N}_2$	22e	223–224	11.60f	11.39
(X)	7- $\text{CH}_3$	4'- $\text{CH}_3$	$\text{C}_{13}\text{H}_{14}\text{O}_3\text{N}_2$	33g	243–244	11.57	11.39
(XI)	6-Cl	5'-Cl	$\text{C}_{12}\text{H}_{11}\text{O}_3\text{N}_2\text{Cl}$	63	250–251	10.69	10.51
(XII)	7- $\text{CH}_3\text{O}$	4'- $\text{CH}_3\text{O}$	$\text{C}_{13}\text{H}_{14}\text{O}_4\text{N}_2$	37h	253–254	10.90	10.69
(XIII)	6- $\text{NO}_2$	5'- $\text{NO}_2$	$\text{C}_{12}\text{H}_{11}\text{O}_3\text{N}_3$	55i	282	15.03	15.16
(XIV)	6,8-Br	3',5'-Br	$\text{Cl}_2\text{H}_{10}\text{O}_3\text{N}_2\text{Br}_2$	57k	286	7.09 <sup>1</sup>	7.19

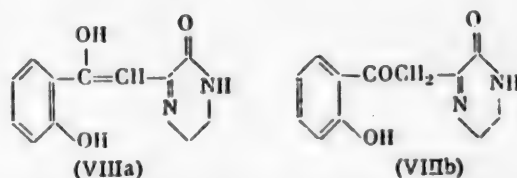
a) In the preparation of piperazinones (VIII, XI–XIV) ethyl esters were used; for piperazinones (IX, X), methyl esters; b) yields for substances (VIII, X, XIV) by method B, for substances (XI–XIII), by method A (see experimental section); c) substances (VIII–XII) for analysis were recrystallized from alcohol, substances (IX, X, and XII) being previously reprecipitated by acetic acid from solution in dilute NaOH. Piperazinones (XIII and XIV) decompose on melting (from nitrobenzene and butanol respectively); d) Found %: C 62.19; H 5.37. Calculated %: C 62.15; H 5.21; e) The crude product was washed with alcohol and ether, and recrystallized from alcohol. A small amount of a colorless substance with m. p.  $> 300^\circ$  separated from the mother liquor on standing; f) Found %: C 63.80; H 5.65. Calculated %: C 63.44; H 5.73; g) the reaction product was treated with alcohol and ether; h) by method B, yield of crude product was 36%, recrystallized from alcohol, 25%; i) the crude product (yield 68%) was purified by treatment with boiling alcohol; k) by method A [the crude product (72%) was purified by recrystallizing from alcohol]; yield 52%. 1) Found %: Br 41.35. Calculated %: Br 40.98.

Piperazinones (XI, XIII, and XIV) are not accompanied by high-melting by-products even when the reaction is carried out in relatively small volumes of solvent (alcohol). It is true that this phenomenon can be explained not only by the influence of the substituents in the 2-carbalkoxychromones but also by the low solubility

of the esters in question, and consequently by their low concentration in solution. In the reaction products with the ester of 6-methylchromonecarboxylic there are always high-melting impurities.

Piperazinones (VIII-XIV) have a golden-yellow tone, are soluble in alkalis (in alkaline solution they undergo gradual rupture); with ferric chloride they give the color reaction characteristic of phenols. On boiling with mineral acids (VIII) is converted into the initial chromonecarboxylic-2 acid.

To 3-(2'-hydroxybenzoylmethylene)-piperazinone-2 (VIII), as well as to the substituted piperazinones, can be ascribed several tautomeric forms, for instance (VIII a) or (VIII b).



In our opinion the most likely form (under ordinary conditions) is the enamino-ketone one (VIII). Form (VIII), because of the structure of the fragment  $\text{--COCH=CNH--}$ , corresponds to the  $\beta$ -aminovinyl ketones.\* As in aminovinyl ketones [10], in piperazinone (VIII) the properties of the carbonyl group and the double bond are suppressed: The compound does not form an oxime, semicarbazone, or p-nitrophenylhydrazone (under conditions usual for o-hydroxyacetophenone, for instance); it is not hydrogenated over a palladium catalyst (760 mm, 20°, in alcohol). It is natural that the basic properties of the amino group should also be considerably weakened, as is evidenced by the absence of salt-forming ability when treated with dilute mineral acids.

#### EXPERIMENTAL

Preparation of substituted chromonecarboxylic-2 acids and their esters is described in a previous work [11].

**Acids (I-VII).** 0.01 mole of the corresponding chromonecarboxylic-2 acid and 1.5 g of hydrazine hydrate in 10 ml of alcohol were boiled for 1 hr [in the case of acid (VII): 3 g of hydrazine hydrate, 30 ml of alcohol, 3 hrs heating]. The alcohol was distilled off in vacuo, the residue treated with dilute hydrochloric acid and dissolved in aqueous  $\text{NaHCO}_3$  (acids II, V, and VII: in soda). The substituted pyrazolecarboxylic acid was precipitated from the filtered solution by addition of conc. HCl, then washed with water and dried over  $\text{CaCl}_2$  and NaOH in a vacuum desiccator. With ferric chloride, acids (I-VII) gave the coloration characteristic for phenolic hydroxyl.

0.55 g of the hydrazide of acid (I) [5] in 5 ml of 2 N NaOH was boiled for 1 hr, and 0.3 g of acid (I) precipitated by acidification, m. p. 234-235°. A sample mixed with a sample of the acid prepared as described above gave no melting point depression. Acid hydrolysis of the hydrazide was very difficult.

#### Piperazinone (VIII)

**Method A.** To a hot solution of 5.45 g of the ethyl ester of chromonecarboxylic-2 acid in 6 ml of alcohol, 2.15 g of ethylenediamine in 4 ml of alcohol was added. The mixture was boiled for 1.5 hrs and then cooled. The precipitate was filtered off, carefully washed in turn with 2 N HCl and water, and dried in a vacuum desiccator over  $\text{P}_2\text{O}_5$ . The crude product (3.1 g) was dissolved in alcohol, filtered from the insoluble yellow precipitate (0.12 g), and on cooling the solution 2.1 g of piperazinone (VIII) obtained with m. p. 212-214°. A further 0.25 g of the same substance was isolated from the mother liquor. Total yield 2.35 g (40%). An almost colorless hydrochloride of undetermined structure separated from the acidic wash solutions on standing. The reaction by-product was insoluble in alcohol; it was treated with boiling alcohol and recrystallized from nitrobenzene, m. p. 352° (with decomp.),  $\lambda_{\text{max}}$  236 m $\mu$  ( $\epsilon$  = 34850) and 306 m $\mu$  ( $\epsilon$  = 12600) (in alcohol). For the unsubstituted amide of the chromonecarboxylic acid  $\lambda_{\text{max}}$  was 236 m $\mu$  ( $\epsilon$  = 23400) and 307 m $\mu$  ( $\epsilon$  = 6860) (in alcohol).

Found %: C 64.75; H 4.07; N 7.05.  $\text{C}_{22}\text{H}_{16}\text{O}_6\text{N}_2$ . Calculated %: C 65.34; H 3.99; N 6.93.

\* For tautomerism of aminovinyl ketones see [9].

The substance was very poorly soluble in organic solvents, insoluble in aqueous NaOH, and did not give a coloration with  $\text{FeCl}_3$  in alcohol.

**Method B.** To a hot solution 1.09 g of the ethyl ester of chromonecarboxylic-2 acid in 100 ml of alcohol, 0.43 g of ethylenediamine in 10 ml of alcohol was added with vigorous stirring. The reaction mixture was boiled for 1.5 hrs, and the alcohol then distilled off in vacuo. The residue was treated in turn with 2 N HCl and water. 0.56 g of piperazinone (VIII) was obtained with m. p. 212-213°. Data on piperazinones (IX-XIV), obtained by method A or B, are given in Table 2.

0.38 g of p-nitrophenylhydrazine, 0.34 g of o-hydroxyacetophenone, and 12 ml of alcohol were boiled for 1.5 hrs, and 0.48 g of the p-nitrophenylhydrazone of o-hydroxyacetophenone obtained. M. p. 242.5-243.5° (from alcohol).

Found %: N 15.89.  $\text{C}_{14}\text{H}_{19}\text{O}_3\text{N}_3$ . Calculated %: N 15.49.

Dipiperazinone (VIII) was recovered in 83% yield after heating for 6 hr with p-nitrophenylhydrazine in alcohol.

Under the conditions for preparation of piperazinone (VIII) by method A, the ethyl ester of o-hydroxybenzoylpyrrolacemic acid with ethylenediamine gave a yellow substance, not melting up to 420°, exceedingly poorly soluble in organic solvents, including boiling nitrobenzene; with an alcoholic ferric chloride solution the solid substance turned dark brown. On boiling with 2 N NaOH the substance went into solution, from which it was not regenerated on acidification.

#### SUMMARY

1. 3-(2'-Hydroxyphenyl)-pyrazolecarboxylic-5 acids were synthesized by reacting chromonecarboxylic-2 acids with hydrazine hydrate.

2. A study was made of the reaction of esters of chromonecarboxylic-2 acids with ethylenediamine, leading to 3-(2'-hydroxybenzoylmethylene)-piperazinones-2.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. Some or all of this periodical literature may well be available in English translation. A complete list of the cover-to-cover English translations appears at the back of this issue.

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## ETHYLENIMINE DERIVATIVES

### II. ETHYLENIMIDES OF PHOSPHORIC AND THIOPHOSPHORIC ACID

A. A. Kropacheva, V. A. Parshina and S. I. Sergievskaya

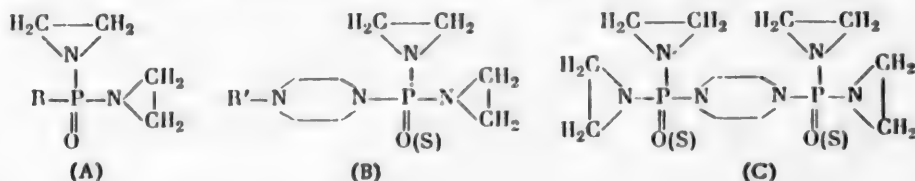
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November, 1960

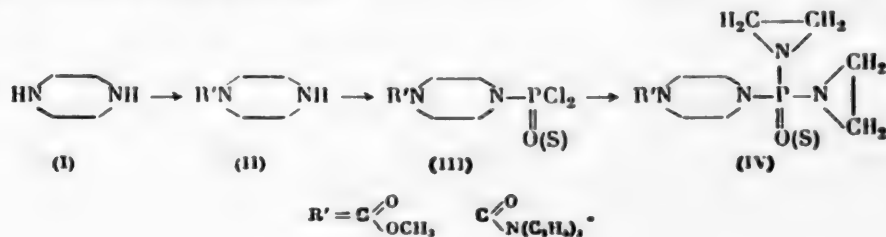
Original article submitted November 16, 1959

In a previous communication [1] the synthesis of diethylenimino derivatives of phosphoric acid of the general formula (A) was described, where R corresponds to an aromatic amino or hydroxy compound. The work described here, which was carried out in 1955, is the commencement of an investigation into ethylenimino derivatives of substituted phosphoric and thiophosphoric acids. This communication describes the production of N,N'-di(ethylene)triamides of phosphoric and thiophosphoric acids, where the R group is substituted or unsubstituted piperazine. In the case of substituted piperazine the compounds which are obtained may be represented by formula (B) and in the case of unsubstituted piperazine, by formula (C).



The synthesis of these compounds was carried out to explain the effect of the substitution of the radical R of formula (A) by the piperazine heterocycle on the physiological activity, as well as the influence of substituents on the nitrogen in the piperazine cycle.

In the first part of the work we give the production of the triamides of phosphoric and thiophosphoric acids containing two ethylenimine groups and a substituted piperazine, i.e., formula (B). These compounds were synthesized via the following series of reactions.



The corresponding N-oxy(thio)chlorophosphines (III) are obtained by this method from the N-monosubstituted piperazines (II), following which the chlorine atoms are substituted by ethylenimine.

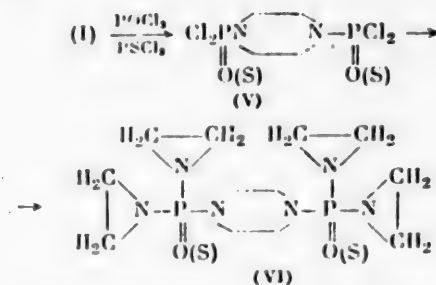
TABLE 1

N-Oxy(thio)chlorophosphines,  $R-N\begin{smallmatrix} CH_2-CH_2 \\ | \quad | \\ CH_2-CH_2 \end{smallmatrix}N-R'$

Expt. No.	R	R'	M.p.	Yield (%)	Solvent for purification	Molecular weight	Formula	% Cl	
								found	calcd.
1	P(O)Cl <sub>2</sub>	COOCH <sub>3</sub>	74-76°	50	C <sub>6</sub> H <sub>6</sub>	261	C <sub>9</sub> H <sub>11</sub> O <sub>3</sub> N <sub>2</sub> P <sub>2</sub> Cl <sub>2</sub>	27.23	27.16
2	P(S)Cl <sub>2</sub>	COOCH <sub>3</sub>	53	64	Ethyl ether	274	C <sub>9</sub> H <sub>11</sub> O <sub>3</sub> N <sub>2</sub> P <sub>2</sub> Cl <sub>2</sub>	25.58	25.58
3	P(O)Cl <sub>2</sub>	CON(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	185° (2 mm)	70.4	Ditto	302	C <sub>9</sub> H <sub>19</sub> O <sub>3</sub> N <sub>2</sub> P <sub>2</sub> Cl <sub>2</sub>	23.5	23.46
4	P(S)Cl <sub>2</sub>	CON(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	72	60	Ethyl ether + petroleum ether	318	C <sub>9</sub> H <sub>19</sub> O <sub>3</sub> N <sub>2</sub> P <sub>2</sub> Cl <sub>2</sub>	22.19	22.3
5	P(O)Cl <sub>2</sub>	P(O)Cl <sub>2</sub>	175	79	CHCl <sub>3</sub> + C <sub>6</sub> H <sub>6</sub>	319	C <sub>9</sub> H <sub>11</sub> O <sub>3</sub> N <sub>2</sub> P <sub>2</sub> Cl <sub>4</sub>	44.49	44.33
6	P(S)Cl <sub>2</sub>	P(S)Cl <sub>2</sub>	160	72.8	C <sub>6</sub> H <sub>6</sub>	352	C <sub>9</sub> H <sub>19</sub> N <sub>2</sub> P <sub>2</sub> S <sub>2</sub> Cl <sub>4</sub>	40.14	40.00

The N-monosubstituted piperazines the carbomethoxy and diethylcarbamoyl piperazines (II) — were obtained by methods already described in the literature [2, 3]. The synthesis of N-oxy(thio)chlorophosphines (III) was carried out by the reaction of carbomethoxy- and diethylcarbamoyl piperazines with phosphorus oxychloride or phosphorus trichloride in a cooled organic solvent, N-(Oxy(thio)chlorophosphine on reacting with ethylenimine in an organic solvent in the presence of triethylamine gave the corresponding ethylenimino derivatives (IV).

In the later part of the work we synthesized phosphoric and thiophosphoric acid triamides containing the ethylenimine and the unsubstituted piperazine groups, i.e., formula (C). The following method was used to obtain these compounds.



By this method we obtained bis-N-oxy(thio)chlorophosphine piperazine (V) from piperazine (I), and then by substituting the chlorine in the chlorophosphine group by ethylenimine we obtained compound (VI). We obtained 1,4-bis-(N-oxychlorophosphine)-piperazine by boiling piperazine hydrochloride with phosphorus oxychloride, and 1,4-bis-(N-thiochlorophosphine)-piperazine by the action of phosphorus thiochloride on piperazine in a cooled organic solvent. Ethylenimino derivatives were obtained as a result of the reaction of the corresponding chlorophosphines with ethylenimine. The reaction was carried out in a cooled organic solvent, in the presence of triethylamine. All the N-oxy(thio)chlorophosphines obtained and their properties are given in Table 1, and the corresponding ethylenimino derivatives in Table 2.

Data on the biological properties of some of the compounds (Nos. 3-6, Table 2) were published earlier [4]. Compound No. 5 (Table 2), known as "dipine," was submitted to an extensive biological study, followed by a clinical investigation. The data of the biological investigation have already been published [5].

## EXPERIMENTAL

The production of N-oxy(thio)chlorophosphines. 1. 1,4-(Carbomethoxy)-(N-oxychlorophosphine)-piperazine. A solution of 7.2 g (0.05 mole) of carbomethoxypiperazine in 30 ml of dry ether was added to a solution of 3.8 grams

TABLE 2

Ethylenimine Derivatives,  $R-N \begin{array}{c} \diagup \\ \diagdown \end{array} N-R'$

Expt. No.	R	R'	M.p.	Yield (%)	Solvent for purification	Molecular weight	Formula	Found %			Calculated %		
								C	H	N	C	H	N
1	$PO \left( N \begin{array}{c} CH_2 \\   \\ CH_2 \end{array} \right)_2$	$COOCH_3$	106—107°	71	Ethyl acetate	274	$C_{10}H_{10}O_3N_4P$	43.98	7.04	43.75	6.98		
2	$PS \left( N \begin{array}{c} CH_2 \\   \\ CH_2 \end{array} \right)_2$	$COOCH_3$	96—97	70	Ditto	290	$C_{11}H_{10}O_3N_4PS$	41.09	6.54	41.36	6.39		
3	$PO \left( N \begin{array}{c} CH_2 \\   \\ CH_2 \end{array} \right)_2$	$CON(C_2H_5)_2$	59	72	Crystallized from hexane	315	$C_{13}H_{26}O_2N_4P$	49.19	8.22	49.5	8.25		
4	$PS \left( N \begin{array}{c} CH_2 \\   \\ CH_2 \end{array} \right)_2$	$CON(C_2H_5)_2$	78—80	72.7	Ditto	331	$C_{13}H_{26}ON_4PS$	47.37	8.02	47.11	7.90		
5	$PO \left( N \begin{array}{c} CH_2 \\   \\ CH_2 \end{array} \right)_2$	$PO \left( N \begin{array}{c} CH_2 \\   \\ CH_2 \end{array} \right)_2$	187	75.5	Crystallized from benzene	346	$C_{12}H_{24}O_4N_6P_2$	41.29	6.92	41.6	6.98		
6	$PS \left( N \begin{array}{c} CH_2 \\   \\ CH_2 \end{array} \right)_2$	$PS \left( N \begin{array}{c} CH_2 \\   \\ CH_2 \end{array} \right)_2$	203	83	Ditto	378	$C_{12}H_{24}N_6P_2S_2$	37.98	6.33	38.1	6.4		

Note: In obtaining compounds 1–5 the reaction was carried out in benzene and compound 6, in chlorobenzene.



(0.025 mole) of freshly distilled phosphorus oxychloride at 6-8°. The reaction mixture was stirred without cooling for 2 hrs, the carbomethoxypiperazine hydrochloride which precipitated was filtered off, and the ether was distilled off under reduced pressure. After removing the solvent, 4.2 g (about 60%) of colorless material was obtained, which was purified by dissolving in benzene. The turbid solution obtained was shaken with carbon, filtered, and evaporated to dryness under vacuum. This process of solution and evaporation was repeated until the solution of the material in benzene was no longer turbid. The transparent solution was evaporated down; 3.5 g of a substance (59%, calculated on the carbomethoxypiperazine) in the form of colorless crystals was obtained.

2. 1,4-(Carbomethoxy)-(N-thiochlorophosphine)-piperazine was obtained in a manner similar to the N-oxy compound, by the action of phosphorus thiochloride on carbomethoxypiperazine (No. 2, Table 1).

3. 1,4-(N-Oxychlorophosphine)-(diethylcarbamoyl)-piperazine. A solution of 7 g (0.04 mole) of diethylcarbamoyl piperazine in 30 ml of absolute ether was added to a solution of 3.06 g (0.02 mole) of phosphorus oxychloride in 20 ml of absolute ether, with mixing and cooling (0-2°). After the reagent had been added, cooling was discontinued, and the reaction mixture was stirred for another two to three hours. The precipitate of diethylcarbamoyl piperazine hydrochloride was filtered off, and the ether distilled from the filtrate. The residue, a viscous liquid, was distilled at 2 mm; the main fraction boiling at 185° was a thick colorless liquid, which from the chlorine analysis corresponded to 1,4-(N-oxychlorophosphine)-(diethylcarbamoyl)-piperazine (No. 3, Table 1). Eight grams was obtained (70% calculated on the basis of diethylcarbamoylpiperazine).

4. 1,4-(N-Thiochlorophosphine)-(diethylcarbamoyl)-piperazine was obtained by the action of phosphorus thiochloride on diethylcarbamoyl piperazine, under conditions analogous to those required in the production of N-oxychlorophosphine. After distilling off the solvent a solid material was formed, which was dissolved in anhydrous benzene. The benzene solution was shaken with carbon, filtered, and the benzene distilled off under vacuum. The residue was recrystallized from a mixture of ethyl and petroleum ethers. A colorless crystalline material, m. p. 72°, was obtained. From the analysis for chlorine the material obtained corresponded to 1,4-(N-thiochlorophosphine)-(diethylcarbamoyl)-piperazine (No. 4, Table 1).

5. 1,4-Bis-(N-oxychlorophosphine)-piperazine. The sample of piperazine dihydrochloride taken was 7.95 g (0.05 mole). This was heated on a gauze with 46 g (0.3 mole) of freshly distilled phosphorus oxychloride until the piperazine dihydrochloride dissolved. The residue was recrystallized from a mixture of chloroform and benzene. It was found that 13.4 g (about 79%, calculated on piperazine) of di-(N-oxychlorophosphine)-piperazine, m. p. 175°, was obtained. The compound is very sensitive to moisture and rapidly evolves hydrogen chloride in air.

6. 1,4-Bis-(N-thiochlorophosphine)-piperazine. A solution of 12.4 g (0.15 mole) of piperazine in 400 ml of dry methylene chloride was gradually added with mixing and cooling (0-5°) to a solution of 25.4 g (0.15 mole) of phosphorus thiochloride in 150 ml of dry methylene chloride. After the reagent had been added, the cooling was discontinued and the reaction mixture stirred for another 4-5 hrs, the piperazine dihydrochloride filtered off, and the methylene chloride distilled from the filtrate under reduced pressure. The residue was recrystallized twice from benzene. The compound was obtained in the form of colorless crystals with m. p. 159-160°. The yield was 18.6 g (78.8%, calculated on piperazine).

The production of ethylenimino derivatives. A weighed batch (5.2 g, 0.02 mole) of 1,4-(carbomethoxy)-(N-oxychlorophosphine)-piperazine was added with mixing and cooling (+5° to -6°) to a solution of 1.71 g (0.04 mole) of ethylenimine and 4.04 g (0.04 mole) of triethylamine in 30 ml of dry benzene. The reaction mixture was stirred without cooling for two hours and left until the following day. The triethylamine hydrochloride which precipitated was filtered off and the benzene distilled off under reduced pressure. The residue (5.7 g) had m. p. 100-103°. It was dissolved in ethyl acetate and the solution shaken with carbon and filtered. The clear solution thus obtained was evaporated under reduced pressure to a small volume and cooled. The di-(ethylene)-phosphine-triamide-carbomethoxypiperazine obtained weighed 4.1 g (71% calculating on chlorophosphine) and had m. p. 106-107°.

The ethylenimino derivatives of the remaining chlorophosphines were produced in an analogous manner. The data are given in Table 2.

#### SUMMARY

Six N-oxy(thio)chlorophosphines of piperazine, and six N,N'-di(ethylene)-N"-piperazinetriamides of phosphoric and thiophosphoric acids, none of which had been described in the literature, have been obtained.

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## THE SYNTHESIS OF SOME MANNICH BASE DERIVATIVES OF HYDROQUINONE

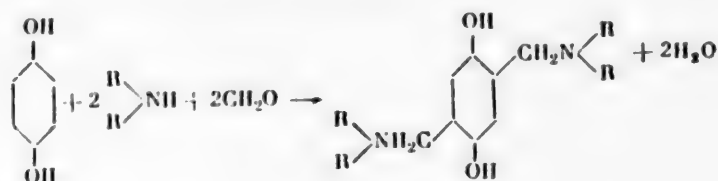
V. A. Bogolyubskii

Translated from *Zhurnal Obshchei Khimii*, Vol. 30, No. 11, pp. 3589-3591,

November, 1960

Original article submitted December 10, 1959

It is known [1-3] that hydroquinone takes part in the Mannich reaction with secondary amines and formaldehyde, forming 2,5-bis(dialkylaminomethyl)-hydroquinones.



Up to the present time only dimethylamine [1], morpholine [2], and diethyl- and di-( $\beta$ -hydroxypropyl)-amine [3] have been used in this reaction.

It appeared to be of interest to synthesize Mannich bases derived from hydroquinone starting from higher molecular weight secondary amines. Such compounds could be used in the production and treatment of moving picture materials [4, 5].

In the present work we have studied the reaction of hydroquinone, formaldehyde, and the secondary amines diethyl-, dipropyl-, dibutyl-, dilsoamyl-, and dilsohexylamines, piperidine, and methyloctadecylamine.

We have obtained the corresponding 2,5-bis(dialkylaminomethyl)-hydroquinones, which are strong bases and give stable salts with mineral and organic acids. In the reaction with alkylating reagents they form poorly crystallizing quaternary salts. All the bases synthesized are strong reducing agents.

### EXPERIMENTAL

#### General Method for Synthesis of 2,5-Bis(dialkylaminomethyl)-hydroquinones

To a water or aqueous alcoholic solution of 1 mole of hydroquinone and 2 moles of the secondary amine with stirring in an atmosphere of nitrogen was added 2 moles of 37% formalin at such a rate that the temperature of the reaction mixture did not exceed 30°. The base which precipitated was filtered on the next day and was recrystallized from alcohol. In some cases the reaction product could best be isolated as the oxalate. For this purpose, we distilled the solvent from the reaction mixture in a vacuum and thus also removed the unreacted amine. The residue was dissolved in acetone and treated with an excess of an acetone solution of oxalic acid. The resulting oxalate crystallized well from aqueous acetone or alcohol. Decomposition of the salt with 10% water solution of soda gave the corresponding base. We thus obtained 2,5-bis(dibutylaminomethyl)- and 2,5-bis(dilsoamylaminomethyl)hydroquinones.

Name	Amount of hydroquinone, g	Amount of 37% formalin, ml	Secondary amine and amount, g	Solvent, ml	Yield, %	M.p.	M.p. of oxalate (with decomposition)	Found N, %	Empirical formula	Calculated N, %
2,5-Bis(diethylaminoethyl)-hydroquinone	22	30	Diethylamine 29.2	Water 40	75.5	106°	192—195°	10.07, 9.96	$C_{18}H_{25}O_2N_2$	99.9
2,5-Bis(dipropylaminomethyl)-hydroquinone	22	30	Dipropylamine 40.4	Water 75	32.3	66	179—180	8.13, 8.32	$C_{20}H_{30}O_2N_2$	8.32
2,5-Bis(dibutylaminomethyl)-hydroquinone	4.7	6.5	Dibutylamine 11	75% alcohol 20	45 •	41	198—199	7.23, 7.09	$C_{24}H_{44}O_2N_2$	7.13
2,5-Bis(disoamylaminomethyl)-hydroquinone	3.34	4.5	Disoamylamine 9.6	75% alcohol 20	46.2 •	63	170—180	6.34, 6.39	$C_{28}H_{52}O_2N_2$	6.24
2,5-Bis(diisohexylaminomethyl)-hydroquinone	5.5	7.5	Diisohexylamine 18.5	Water 35	10.3 ••	80	—	5.60, 5.55	$C_{32}H_{58}O_2N_2$	5.57
2,5-Bis(dipiperidinomethyl)-hydroquinone	11	15	Piperidine 17	Water 50	84.1	190	215—220	9.38, 9.18	$C_{18}H_{28}O_2N_2$	9.20
2,5-Bis(methyloctadecylaminomethyl)-hydroquinone	22	30	Methyloctadecylamine 112.8	Benzene 200 Water 40	65	87	180—184	4.19, 4.30	$C_{46}H_{98}O_2N_2$	3.99

• Isolated as the oxalate with later decomposition by 10% soda solution. Yield given calculated on the free base.

•• Crystallized out from the reaction mass on long standing.

2,5-Bis(dibutylaminomethyl)hydroquinone. To a solution of 4.7 g (0.043 mole) of hydroquinone and 11 g (0.086 mole) of dibutylamine in 20 ml of 75% alcohol, with stirring, in an atmosphere of nitrogen, was added 6.5 ml (0.086 mole) of formalin at such a rate that the temperature of the reaction mass did not exceed 30°. After distillation of the solvent and unreacted amine in vacuum, the residue was dissolved in 50 ml of acetone, and a solution of 10.8 g of oxalic acid in 50 ml of acetone was added. The precipitated salt was recrystallized from aqueous acetone. Yield 13.65 g (66.7%), m. p. 198-199° (with decomposition).

Two g of 2,5-bis(dibutylaminomethyl)hydroquinone oxalate in 40 ml of water was treated with 5 ml of a 10% soda solution. The precipitated base was recrystallized from alcohol. Large colorless crystals with m. p. 41°. Yield 1.1 g (70%). In the table we give the conditions of synthesis and results of analysis of the 2,5-bis-(dialkylaminomethyl)hydroquinones which were obtained.

#### SUMMARY

The Mannich reaction of hydroquinone with secondary amines and formaldehyde gave seven new bases.

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# STUDIES OF THE PROPERTIES OF AMINO ACIDS AND PEPTIDES WHICH CONTAIN TERTIARY NITROGEN ATOMS

## IV. THE SYNTHESIS OF SOME PEPTIDES WHICH CONTAIN TERTIARY NITROGEN ATOMS

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Moscow State University

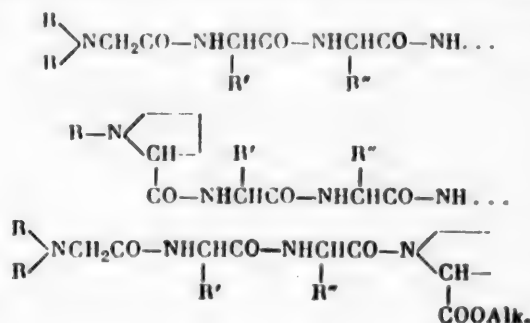
Translated from *Zhurnal Obshchei Khimii*, Vol. 30, No. 11, pp. 3591-3598,

November, 1960

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In a previous communication [1] we showed especially the effect of two benzyl groups on a nitrogen atom on the stability of N,N-dibenzyl- $\alpha$ -amino acid chlorides, and also the ability of N,N-dibenzyltripeptides to show special behavior in the formation of the copper biuret complex.

In this study we have continued the synthesis of peptides with tertiary nitrogen atoms placed in the compound with terminal tertiary nitrogen atoms which have various protective groups, and with tertiary nitrogen atoms so built into the peptide molecule that they can be represented as follows:



The synthesis of these peptides was carried out for a study of their behavior in the formation of copper complexes depending on the peptide structure. The peptides synthesized are given in Tables 1 and 2.

The esters of N,N-dibenzyltripeptides were obtained by the method of mixed anhydrides [2]. The method in most cases was changed at the stage of purifying the substances. While dibenzylleucine was not soluble in hydrochloric acid and dissolved well in chloroform, dibenzylglycine dissolved in hydrochloric acid, but poorly in chloroform, and therefore after carrying out the reaction in the case of dibenzylleucine derivatives the chloroform solution was washed with dilute hydrochloric acid, with water, and with 2 N soda, in which dibenzylleucine is easily soluble, and again with water. After the reaction, the chloroform was evaporated dry and the remaining oil was treated with water (which removed the triethylamine hydrochloride) or was precipitated from alcohol by water. The oil usually crystallized well on standing in the cold and stirring with a rod. The resulting crystals were filtered and washed with absolute ether and ligroin. We should remark that esters of dibenzyl-dipeptides crystallize worse than do esters of dibenzyltripeptides (especially leucine derivatives).



TABLE 1

Name	Yield, %	M. p.	R <sub>f</sub> (butanol-water-CH <sub>3</sub> COOH)
Ethyl ester of carbobenzoxy-dl-prolyl-glycyl-glycine	66.9	93*	0.84
Carbobenzoxy-dl-prolyl-glycyl-glycine	81	109	0.5
N-Benzyl-dl-proline	34	102 (decomp.)	0.8
Ethyl ester of N-benzyl-dl-propyl-glycyl-glycine	54	75	0.7
Ethyl ester of dl-prolyl-glycyl-glycine hydrochloride	61	Oil	0.47
dl-Prolyl-glycyl-glycine (hydrochloride)	75	The same	0.28
Methyl ester of N,N-dibenzylglycyl-glycyl-glycyl-proline	60.3	68	0.9
Methyl ester of glycyl-glycyl-glycyl-dl-proline	55	128 (decomp.)	0.37
Ethyl ester of N,N-dibenzylglycyl-glycyl-glycine	68.7	78	0.8
N,N-Dibenzyl-diglycyl-glycine	66	157-158	0.15
N,N-Diethylleucyl-glycyl-glycine (hydrochloride)	57.3	Oil	0.54

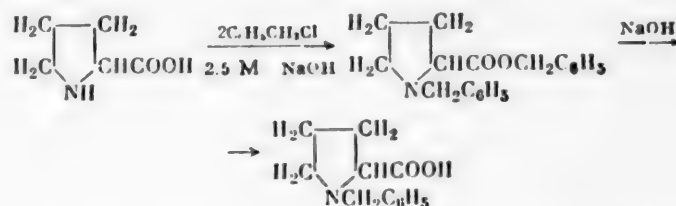
TABLE 2

Name	Yield, %	M. p.	Shifted (in cm) to the cathode in electrophoresis at potential gradient	
			6.6 in 3 hours	22.05 after 3 hours
Ethyl ester of N,N-dibenzyl-glycyl-glycine	73	77-78*	5.5 (4.15)	4.3
N,N-Dibenzylglycyl-glycine	92	157-158*	5.1 (4.15)	4.75
N,N-Dibenzylglycyl-glycyl-glycine hydrochloride	—	170	—	3.9
Ethyl ester of N,N-dibenzyl-leucyl-glycine	82.5	96.5	—	4.2
N,N-Dibenzylleucyl-glycine	60	140	3.05 (3)	—
Methyl ester of N,N-dibenzyl-leucyl-glycyl-leucine	63	127	3.0 (4.3)	3.2
Methyl ester of N,N-dibenzyl-leucyl-glycyl-phenylalanine	66	151	—	3.3

\* According to the literature, oil with b. p. 245°.

The dibenzylpeptides were obtained by saponification of the esters, and purification was sufficiently easy, but here we should note the fact that the dibenzylpeptides are amphoteric compounds. Therefore, depending on the pH of the medium they can be isolated as Na salts of the dibenzylpeptide, as the free dibenzylpeptide, or as its hydrochloride (if the neutralization is carried out with hydrochloric acid). The sodium salt of the

dibenzylpeptide was isolated from a nearly neutral medium (pH 6.8-7.0), the dibenzylpeptide at pH of about 5.5 to 6.2. In a strongly acid medium with standing, the dibenzylpeptide hydrochlorides separate in the form of characteristic needle shaped crystals. In the separation of the dibenzylpeptides it is useful first to distill off the alcohol partially in a vacuum and then carry out the neutralization. N-Benzylproline was synthesized by the method of Vellus [3] as modified by Poddubnaya and Maksimov [1] for N,N-dibenzylleucine by the scheme:



Saponification of the benzyl ester of N-benzylproline occurred completely using live steam (120°) for the distillation of the benzyl alcohol. Under more severe conditions there was a strong tarring of the substance, and under milder ones a large admixture of ester remained. In the separation of N-benzylproline it was necessary to acidify carefully to an acid reaction to Congo, since otherwise the Na salt of N-benzylproline separated; it was obtained chromatographically homogeneous and analytically pure after reprecipitation by ether from alcohol at -40°. To purify the N-benzylproline from inorganic salts, the precipitate was best treated several times with anhydrous chloroform, after removal of which the substance was recrystallized from absolute ether. Reprecipitation from chloroform or from alcohol by ether was accompanied by much loss, and, though the substance obtained chromatographically homogeneous, we did not get it in an analytically pure state.

The synthesis of the ethyl ester was carried out with the N-benzylproline which we obtained, using the method of mixed anhydrides. After recrystallization from hot water the substance was obtained chromatographically and analytically homogeneous. All the chromatographic studies were run in the system butanol-acetic acid-water (4:1:5). Saponification of the ethyl ester of carbobenzoxy-dl-prolyl-glycyl-glycine had to be carried out carefully, since in comparison with the other peptides, hydrolysis of the peptide bond of this peptide occurred much more easily (saponification was carried out as described for the ethyl ester of phenylalanyl-proline [4]). Thus, using 20% excess of 1 N sodium hydroxide for 20 hours there was easy hydrolysis of the peptide at the prolyl-glycine bond. On the chromatogram we observed the appearance of spots with R<sub>f</sub> corresponding to glycyl-glycine and proline. It was better to saponify the tripeptide ethyl ester before removal of the carbobenzoxy group.

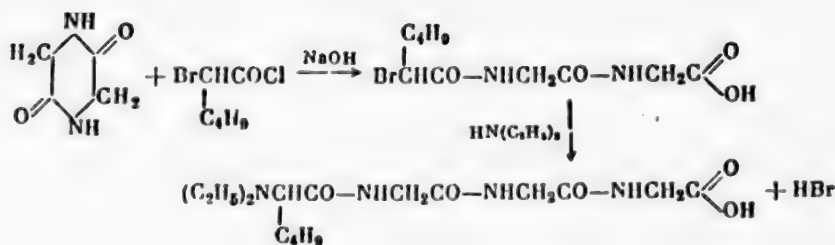
The synthesis of the tetrapeptide, methyl ester of N,N-dibenzylglycyl-glycyl-glycyl-proline, was carried out by joining dibenzyltriglycine with the hydrochloride of the methyl ester of proline by the method of mixed anhydrides. It should be noted that for the success of this reaction the conditions for the formation of the mixed anhydrides are of the greatest value. Thus the most successful method of getting a good yield of substance is keeping the mixed anhydride for 15 minutes at -8°. With longer standing, even at -10° decomposition of the mixed anhydride begins and so the yield is decreased. After purification, the substance is obtained crystalline, and by chromatography is homogeneous. On hydrolysis of the dibenzyltetrapeptide with 20% hydrochloric acid for eight hours, proline and glycine are found. The chromatogram of the hydrolyzate was developed with benzidine, ninhydrin, and isatin (proline gives a blue spot and glycine a pink one).

The ease of removing the dibenzyl protective groups was once more confirmed in obtaining the tetrapeptide. By hydrogenation with Pd black in acetic acid at 50° for three hours we were able to obtain the methyl ester of the tetrapeptide with a yield of 55%.

N, N-Diethyllorleucyl-glycyl-glycine was synthesized by analogy with the method described in the literature [5] for N,N-diethylleucyl ester (see next page).

The optimum conditions for alkylation were to keep with a fivefold excess of diethylamine for 30 days. The substance was isolated as the hydrochloride, which was chromatographically and analytically homogeneous.

All of the compounds which we obtained were studied for their ability to form a copper complex, and, as we reported earlier, we found that the effect of a dialkyl protective group on the nitrogen atom tended to double the complex formation, and in the case of acyl protective groups there was inhibition of the ability to give the biuret reaction.



## EXPERIMENTAL

dl-Proline\* was obtained by the method described in the literature [6]: yield 10.5 g (42.3%). M. p. 202°; according to the literature 202-203°.

N-Carbobenzyloxy-dl-proline was obtained by the method of E. Abderhalden [8]. Yield 9 g (84%). Non-crystallizing oil.

Found %: N 5.72, 5.79.  $\text{C}_{13}\text{H}_{15}\text{O}_4\text{N}$ . Calculated %: N 5.62.

Methyl dl-prolinate hydrochloride was obtained by analogy with the method for methyl dl-prolinate [9]. Yield 2.1 g (73.6%). M. p. 76°. The hydrochloride of methyl dl-prolinate is described in the literature; no melting point is given [7].

N-Benzyl-dl-proline. Two g of dl-proline was dissolved in 20 ml of ethanol; 4.42 g of freshly distilled benzyl chloride was added, as was a solution of 2 g of sodium hydroxide in 7 ml of water. The mixture was heated on a water bath for three hours. The benzyl alcohol was distilled off with live steam during six hours, and 5 g of sodium hydroxide was added to the reaction mixture. The precipitated sodium chloride was filtered off. It was acidified with acetic acid to an acid reaction. The acid solution was evaporated dry in a vacuum. The dry residue was extracted with 100 ml of absolute chloroform. The chloroform was distilled off in a vacuum. To remove the excess acetic acid we treated it several times with anhydrous toluene and evaporated in a vacuum. The oil obtained in this way was crystallized under absolute ether. The ester, three times reprecipitated from alcohol by ether at -40°, gave a pure crystalline substance, though purification was accompanied by great loss. Yield before reprecipitation 2.4 g (68%); after reprecipitation, 1.2 g (34%), m. p. 102° (decomposition). Not described in the literature.

Found %: C 63.67, 63.38; H 6.04, 6.05.  $\text{C}_{12}\text{H}_{14}\text{O}_2\text{NNa}$ . Calculated %: C 63.43; H 6.17.

N-Benzylproline dissolved in methyl and ethyl alcohols, dioxane, acetone, ethyl acetate, water, and chloroform; it did not dissolve in benzene, toluene, carbon tetrachloride, ether, and ligroin.

Ethyl ester of N-benzyl-dl-prolyl-glycyl-glycine. One g of N-benzyl-dl-proline in 10 ml of anhydrous chloroform was cooled to -10°, and 0.74 ml of triethylamine and 0.45 ml of ethyl chlorocarbonate were added; during 15 minutes at -9° with shaking we added to the mixture a solution of 1.2 g of ethyl glycyl-glycinate hydrochloride with 0.88 ml of triethylamine in 25 ml of chloroform. The solution stood for one hour at 0° and then overnight at room temperature. It was washed repeatedly with water, and the chloroform was removed in a vacuum. The resulting oil was dissolved several times in anhydrous alcohol and the solvent was distilled. It was recrystallized from hot water. Yield 0.92 g (54%). M. p. 75°. The substance was obtained for the first time.

Found %: C 62.34, 62.42; H 7.28, 7.33.  $\text{C}_{18}\text{H}_{25}\text{O}_4\text{N}_3$ . Calculated %: C 62.24; H 7.20.

Soluble in alcohol, acetone, acetic acid, ethyl acetate; partly soluble in ether, benzene, and water (with heating); insoluble in ligroin. It gives a positive biuret reaction with different absorption maxima depending on the concentration of alkali.

\* Also obtained from  $\alpha$ -chlorocarboxypiperidone according to the method of the literature [7]. The yield of proline hydrochloride was 62 g (41%). Free proline was obtained by purification on resin KU-2. The yield of dl-proline was 25 g from 40 g of hydrochloride (83.5%). M. p. 202°.

Ethyl ester of N,N-dibenzylglycyl-glycyl-glycine. Three g of N,N-dibenzylglycine was dissolved in 50 ml of anhydrous chloroform and 1.62 ml of triethylamine with careful heating on a water bath; the mixture was cooled to  $-10^{\circ}$  and treated with 1.2 ml of ethyl chlorocarbonate; after 30 minutes we added 3 g of the hydrochloride of ethyl glycylglycinate in 60 ml of absolute chloroform and 3 ml of triethylamine with stirring. The mixture stood overnight at room temperature. The chloroform was distilled off in a vacuum, and the substance was recrystallized by precipitation from alcohol with water. Yield 3.4 g (73%). M. p.  $77-78^{\circ}$ . Not described in the literature.

Found %: C 66.43, 66.42; H 7.02, 7.13; N 10.43, 10.57.  $C_{22}H_{27}O_4N_3$ . Calculated %: C 66.49; H 6.80; N 10.57.

A white, crystalline substance, easily soluble in methanol, chloroform, acetone, benzene, and other organic solvents; entirely insoluble in water, soda solution, ether, ligroin and isoamyl alcohol. Electrophoretically homogeneous.

N,N-Dibenzylglycyl-glycyl-glycine. We dissolved 2.2 g of ethyl ester of N,N-dibenzylglycyl-glycyl-glycine in 3.3 ml of methanol. To the resulting solution we added 7.0 ml (25% excess) of 2 N alkali and the mixture stood overnight. The excess alkali was neutralized with 2 N hydrochloric acid to the appearance of turbidity, and the solution was left at room temperature for a day. The finely crystalline precipitate was filtered off and washed several times with water and absolute ethyl ether. Yield 1.3 g (92%), m. p.  $157-158^{\circ}$ . Described in the literature as an oil [10] (from N,N-dibenzylglycyl chloride), and by other authors as melting at  $245^{\circ}$  [11].

Found %: C 65.04, 65.03; H 6.23, 6.16.  $C_{20}H_{23}O_4N_3$ . Calculated %: C 65.04; H 6.23.

Easily soluble in methanol, chloroform, carbon tetrachloride, dioxane, and other organic solvents, not soluble in water, dilute hydrochloric acid, ether, ethyl acetate, and amyl alcohol. Electrophoretically and chromatographically homogeneous.

Ethyl ester of N,N-dibenzylleucyl-glycine. The synthesis was carried out starting from 2.1 g of N,N-dibenzylleucine under the conditions described for the synthesis of the triglycine derivative. The chloroform solution after the reaction was washed four times with 1 N NaOH (60% of the volume), with water, twice with a solution of 2 N soda, and again with water. The solution was dried over fused sodium sulfate. The chloroform was distilled off in a vacuum, and the substance was purified by reprecipitation from alcohol with water. The oil which formed was crystallized by standing in the cold. Yield 3.25 g (82.5%), m. p.  $96.5^{\circ}$ . Not described in the literature.

Found %: C 66.76, 66.72; H 7.77, 7.79; N 6.20, 6.40.  $C_{24}H_{33}O_3N_2Cl$ . Calculated %: C 66.70; H 7.63; N 6.48.

N,N-Dibenzylleucyl-glycine. Saponification of the ester was carried out as described above with use of 24% excess of 2 N alkali. To the oil which precipitated after neutralization we added dilute hydrochloric acid. The crystals were filtered off, washed with a small amount of water and ligroin. Yield of hydrochloride 0.66 g (60%), m. p.  $140^{\circ}$ . Not described in the literature.

Methyl ester of N,N-dibenzylleucyl-glycyl-leucine was prepared by the above method, starting from 1.01 g of hydrochloride of N,N-dibenzylleucyl-glycine, 0.48 g of ethyl ester of chlorocarbonic acid, and 1.38 g of methyl leucinate hydrochloride. For crystallization the oil was ground for sometime under water with the addition of a small amount of 1 N NaOH, separated from the water and washed with absolute ether. The finely crystalline precipitate of hydrochloride was carefully washed with absolute ether. Yield 0.7 g (66.6%). M. p.  $127^{\circ}$ . Obtained for the first time.

Found %: C 65.97, 65.93; H 7.96, 7.80; N 8.14, 7.98.  $C_{29}H_{42}O_4N_3Cl$ . Calculated %: C 65.47; H 7.93; N 7.93.

Easily soluble in organic solvents; insoluble in water, hydrochloric acid, and ether.

Methyl ether of N,N-dibenzylleucyl-glycyl-phenylalanine was obtained in an analogous way from 1.01 g of the hydrochloride of N,N-dibenzylleucyl-glycine in 25 ml of anhydrous chloroform, 0.69 ml of  $(C_2H_5)_3N$ , and 0.48 ml of ethyl chlorocarbonate. It was combined with 1.62 g of the hydrochloride of the methyl ester of phenylalanine in 35-40 ml of anhydrous chloroform and 1.03 ml of triethylamine. It was isolated as the hydrochloride by analogy with the preceding case.

Found %: C 69.26, 69.10; H 7.09, 7.21; N 7.43, 7.47.  $C_{32}H_{29}O_4N_3 \cdot 1\frac{1}{2}H_2O$ . Calculated %: C 69.03; H 7.01; N 7.55.

Methyl ester of N,N-dibenzylglycyl-glycyl-glycyl-dl-proline. One g of N,N-dibenzylglycyl-glycyl-glycine was dissolved in 15 ml of anhydrous chloroform, and 0.41 ml of triethylamine was added. The solution was cooled to  $-9^\circ$ , and 0.3 ml of chlorocarbonic ester was added. The mixture was kept at  $-8^\circ$  for 15 minutes; then with stirring, a solution of 0.56 g of the hydrochloride of the methyl ester of dl-proline with 0.53 ml of triethylamine in chloroform was added. The mixture was kept for one hour at  $0^\circ$  and then overnight at room temperature. It was washed repeatedly with water, 1 N soda, and then water again. The chloroform was distilled off, and the oil was dried in a vacuum desiccator over alkali. When the oil was dissolved in a small amount of ether it became crystalline after direct precipitation from the absolute ether. For purification it was reprecipitated by water from a minimum amount of alcohol. Characteristic rod shaped crystals. Yield 0.8 g (60.3%). M. p.  $68^\circ$ . Prepared for the first time.

Found %: N 11.42, 11.48.  $C_{26}H_{32}O_5N_4$ . Calculated %: N 11.66.

Soluble in methanol, acetone, benzene, chloroform, acetic acid, ether; not soluble in water and ligroin. The substance was chromatographically homogeneous. It was submitted to eight-hour hydrolysis with 20% hydrochloric acid. The hydrolyzate gave in chromatography in the same system two spots characteristic of glycine ( $R_f$  0.2) and proline ( $R_f$  0.3). The chromatogram was developed with ninhydrin, benzidine, and isatin (blue spot for proline, pink for glycine).

The N, N-dibenzyltetrapeptide gave a positive biuret reaction with different absorption maxima depending on the concentration of alkali.

Methyl ester of glycyl-glycyl-glycyl-dl-proline. We hydrogenated 0.2 g of the methyl ester of N,N-dibenzylglycyl-glycyl-glycyl-dl-proline over 0.05 g of Pd black in 6 ml of 80% acetic acid for 3 hours at  $50^\circ$ . After distillation of the solvent in a vacuum the substance was treated several times with anhydrous toluene, and the solvent was distilled off. The oil rapidly crystallized under absolute ether. It was reprecipitated from alcohol by ether. Yield 0.07 g (55%). M. p.  $128^\circ$  (decomposition). Not described in the literature.

Found %: N 18.82, 19.17.  $C_{12}H_{20}O_5N_4$ . Calculated %: N 18.66.

Soluble in alcohols, benzene; insoluble in water, ether, acetone, ligroin, and chloroform. It gives an intense biuret reaction, which is characteristic of tripeptides.

Hydrochloride of N, N-diethylnorleucyl-glycyl-glycine. A mixture of 6.3 g of n-caproyl-glycyl-glycine and 11 mg of diethylamine in 10 ml of alcohol stood for 30 days. At the end of this period the solution was evaporated in a vacuum to formation of a glassy residue. The residue was dissolved in 20 ml of water, and the solution was made alkaline with sodium hydroxide. The excess diethylamine was repeatedly extracted with ether. The solution was acidified with 20% hydrochloric acid to a weakly acid reaction. The solution was evaporated in a vacuum and precipitated with ether. It was dried over alkali. Yield 3.9 g (57.3%).

Found %: N 12.32, 12.28.  $C_{14}H_{24}O_4N_3Cl$ . Calculated %: N 12.43.

The substance was very hygroscopic; easily soluble in alcohols, chloroform; more difficultly so in acetic acid, acetone; insoluble in benzene, ether, and ligroin. The chromatogram gave one spot with  $R_f$  0.54. The compound gives a positive biuret reaction with different absorption maxima depending on the concentration of alkali.

## SUMMARY

1. We have synthesized the undescribed N,N-dibenzylpeptides: N,N-dibenzylleucyl-glycine; hydrochloride of N,N-dibenzylglycyl-glycyl-glycine; ethyl esters of: N,N-dibenzylleucyl-glycine, N,N-dibenzyl-glycyl-glycyl-glycine, N-benzyl-dl-prolyl-glycyl-glycine, carbobenzoxy-dl-prolyl-glycyl-glycine; and the methyl esters of: N,N-dibenzylleucyl-glycyl-leucine, N,N-dibenzylleucyl-glycyl-phenylalanine, and N,N-dibenzylglycyl-diglycyl-dl-proline.

2. We have obtained the ethyl ester of dl-prolyl-glycyl-glycine and the methyl ester of diglycyl-glycyl-dl-proline.

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# THE REACTIONS OF CHLORINE-CONTAINING TELOMERS OF DIENE HYDROCARBONS

## V. THE SYNTHESIS OF SOME ALCOHOLS OF THE SESQUITERPENE SERIES AND THEIR ANALOGS

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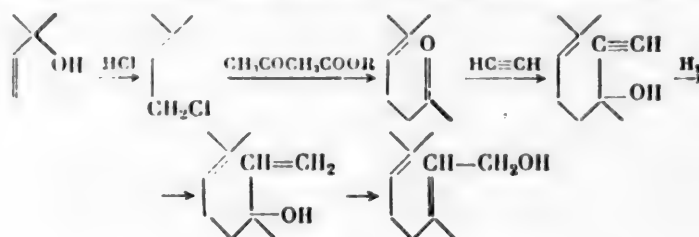
Translated from *Zhurnal Obshchei Khimii*, Vol. 30, No. 11, pp. 3598-3604,

November, 1960

Original article submitted January 1, 1960

In recent years much attention in the literature has been devoted to developing synthetic methods for obtaining terpene, sesquiterpene, and polyterpene alcohols.

The first of these studies was the work of Ruzicka [1, 2], who proposed a general method of synthesis which was then often used by other investigators with some changes in the separate steps [3-8].



For the synthesis of the ketones which are intermediates in this scheme they used the condensation of allyl chlorides with sodium acetoacetic ester and the condensation of the corresponding alcohols with acetoacetic ester or with diketones, with later pyrolysis. For transformation of the ketones into alcohols with an augmented carbon chain, besides ethynylation with acetylene, they carried out vinylation with vinylmagnesium bromide [9] and condensation with bromoacetic ester followed by reduction [10].

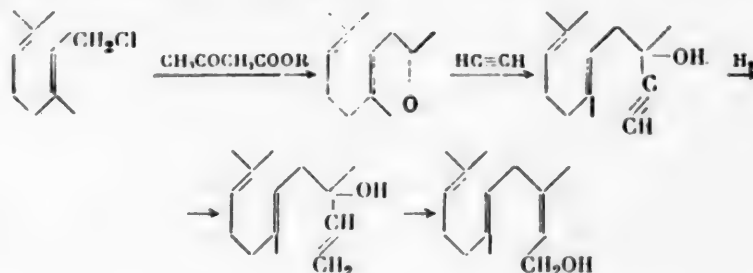
Other schemes were also suggested for synthesis of terpene and sesquiterpene alcohols and their homologs, for example the magnesium organic synthesis with participation of methyl cyclopropyl ketone [11].

In 1958 appeared the report of the use of the Ruzicka scheme for the industrial preparation of terpene, sesqui- and polyterpene alcohols, and also for carotenoids and vitamin A and E. The ketones in this process were obtained with diketene [12].

Because of the successful studies of the telomerization of diene hydrocarbons with halogen derivatives it became easy to obtain terpene, sesquiterpene, and polyterpene chlorides, their analogs and homologs [13-19]. We have attempted to use these chlorides for the synthesis of nerolidol, farnesol, and their homologs and analogs by the classical scheme of Ruzicka.

For this study we took the terpene chlorides obtained by telomerization of prenyl chloride with isoprene (geranyl chloride) and piperylene hydrochloride with isoprene and chloroprene. As was shown earlier, the latter two substances are especially suitable for model investigations since they are obtained in high yield and in a sufficiently pure state [15].

From geranyl chloride we obtained geranyl acetone and from the latter, dehydronerolidol, nerolidol, and farnesol. Dehydronerolidol was purified from the admixed ketones which were seen in the study of its infrared spectrum, although the substance did not differ in its constants from the dehydronerolidol described in the literature. This fact gives us a basis for doubting the purity of many sesquiterpene alcohols described in the literature, if infrared spectra were not used in their investigation.



In an analogous way, from 1-chloro-3,5-dimethyl-2,6-octadiene we obtained 3,7,9-trimethyl-6,10-dodecadien-1-yn-3-ol and 3,7,9-trimethyl-1,5,10-dodecatrien-3-ol, isomers of dehydronerolidol and nerolidol, and from 1,3-dichloro-5-methyl-2,6-octadiene, 7-chloro-3,9-dimethyl-6,10-dodecadien-1-yn-3-ol and 7-chloro-3,9-dimethyl-1,6,10-dodecatrien-3-ol, analogs of the above substances with an atom of chlorine instead of the methyl group.

All these alcohols are oily, colorless liquids with a pleasant odor which at high dilutions resembles the odor of farnesol. They distill at 10 mm without decomposition. The chief constants of these alcohols are given in Table 1.

Table 1 shows that alcohols with a terminal acetylene or vinyl group scarcely differ in boiling point. The latter have a somewhat lower specific gravity and index of refraction.

In the infrared spectra of the alcohols with a terminal acetylenic group the triple bond has a frequency of about  $2120\text{ cm}^{-1}$  (weak) and a valence CH oscillation with an intense frequency of about  $3290\text{ cm}^{-1}$ . The valence frequencies of the double bond in the spectrum of the alcohols which do not contain chlorine have very small intensity. In the spectra of chlorine-containing alcohols the intensity of these frequencies is considerably higher. The deformation CH oscillation in the group  $\text{—C=C—}$  is an intense frequency of  $968\text{ cm}^{-1}$ .

In the infrared spectra of alcohols with the nerolidol grouping there are intense deformation frequencies characteristic for the vinyl group ( $995$  and  $920\text{ cm}^{-1}$ ).

In all the spectra the valence frequencies of the OH bond lie at about  $3400\text{ cm}^{-1}$  and for the OC bond, at about  $1100\text{ cm}^{-1}$ .

## EXPERIMENTAL

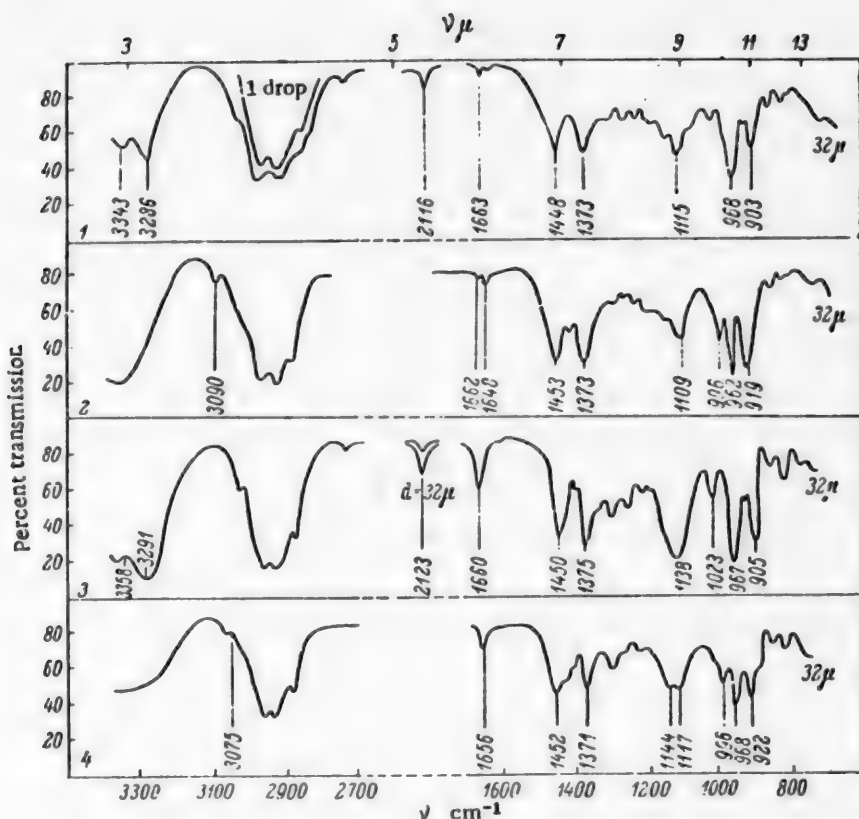
The terpene chlorides were obtained by telomerization of isoprene and chloroprene with hydrochlorides of isoprene and piperylene. Telomerization was carried out at a ratio of diene to hydrochloride of 1:1 in methylene chloride. As a catalyst we used a 5% solution of tin chloride in methylene chloride. The reaction was stopped by addition of pyridine. The constants of the chlorides used are given in Table 2. They scarcely differ from those found previously.

Geranyl acetone and other ketones with analogous structures were obtained by condensation of the telomers shown in Table 2 with sodium acetoacetic ester. The conditions for carrying out this reaction were like those described in one of the preceding communications [20]. The constants of the resulting ketones are given in Table 3. They scarcely differ from those given before.

TABLE 1

Chief Constants of Sesquiterpene Alcohols and Their Analogs

Substance	B.p. (10 mm)	$d_4^{20}$	$n_D^{20}$	MR	
				found	calculated
$\text{CH}_3-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-\text{CH}_2-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-\text{CH}_2-\text{C}(\text{OH})(\text{CH}_3)-\text{C}\equiv\text{CH}$ (I)	123–124° (2.5 mm)	0.8888	1.4798	70.40	70.06
$\text{CH}_3-\text{CH}=\text{CH}-\text{CH}_2-\text{CH}_2-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-\text{CH}_2-\text{C}(\text{OH})(\text{CH}_3)-\text{C}\equiv\text{CH}$ (II)	117–119 (0.6 mm)	0.8886	1.4798 [5]	—	—
$\text{CH}_3-\text{CH}=\text{CH}-\text{CH}_2-\text{CH}_2-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-\text{CH}_2-\text{C}(\text{OH})(\text{CH}_3)-\text{C}\equiv\text{CH}$ (III)	133–134	0.8838	1.4749	70.18	70.06
$\text{CH}_3-\text{CH}=\text{CH}-\text{CH}_2-\text{CH}_2-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-\text{CH}_2-\text{C}(\text{OH})(\text{CH}_3)-\text{C}\equiv\text{CH}$ (IV)	146–147	0.9774	1.4855	70.66	70.31
$\text{CH}_3-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-\text{CH}_2-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-\text{CH}_2-\text{C}(\text{OH})(\text{CH}_3)-\text{CH}=\text{CH}_2$ (V)	123–125 (4 mm) 94	0.8785	1.4783	70.88	71.59
$\text{CH}_3-\text{CH}=\text{CH}-\text{CH}_2-\text{CH}_2-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-\text{CH}_2-\text{C}(\text{OH})(\text{CH}_3)-\text{CH}=\text{CH}_2$ (VI)	(0.18 mm)	0.8752	1.4784 [5]	—	—
$\text{CH}_3-\text{CH}=\text{CH}-\text{CH}_2-\text{CH}_2-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-\text{CH}_2-\text{C}(\text{OH})(\text{CH}_3)-\text{CH}=\text{CH}_2$ (VII)	133–134	0.8711	1.4742	71.37	71.59
$\text{CH}_3-\text{CH}=\text{CH}-\text{CH}_2-\text{CH}_2-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-\text{CH}_2-\text{C}(\text{OH})(\text{CH}_3)-\text{CH}=\text{CH}_2$ (VIII)	143–144	0.9547	1.4840	72.75	71.84
$\text{C}_6\text{H}_5-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-\text{CH}_2-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-\text{CH}_2-\text{C}(\text{OH})(\text{CH}_3)-\text{CH}=\text{CH}_2$ (IX)	142–143 (6 mm)	0.8878	1.4878	72.13	71.59
$\text{C}_6\text{H}_5-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-\text{CH}_2-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-\text{CH}_2-\text{C}(\text{OH})(\text{CH}_3)-\text{CH}=\text{CH}_2$ (X)	126–127 (0.5 mm)	0.8886	1.4870 [5]	—	—



Infrared transmission spectra. 1) 3,7,9-trimethyl-6,10-dodecadien-1-yn-3-ol; 2) 3,7,9-trimethyl-1,6,10-dodecatrien-3-ol; 3) 7-chloro-3,9-dimethyl-6,10-octadien-1-yn-3-ol; 4) 7-chloro-3,9-dimethyl-1,6,10-dodecatrien-3-ol.

Ethynylation of the ketones was carried out in liquid ammonia. As an example of the synthesis we give that of 3,7,9-trimethyl-6,10-dodecadien-1-yn-3-ol.

In a round bottomed flask fitted with a stirrer, dropping funnel, and tubes for inlet and outgo of acetylene and surrounded by a heat insulating cover we placed 350 ml of liquid ammonia. With stirring, in a stream of acetylene we added in small portions 12.5 g of metallic sodium. Then in the course of one hour we added dropwise 47 g of 6,8-dimethyl-6,9-undecadien-2-one, obtained from the telomer of isoprene with piperylene hydrochloride. The reaction mixture was stirred for nine hours and then stood overnight. After evaporation of the ammonia the viscous yellow residue was treated with a solution of 130 ml of concentrated HCl in 400 ml of water mixed with ice. The reaction product was extracted with ether. The ether extract was washed with a saturated solution of sodium bicarbonate and dried over ignited  $\text{MgSO}_4$ . After distillation of the ether, the residue was distilled in a vacuum. We obtained 43 g (78%) of a product with b. p. 109–112° (4 mm),  $n_D^{20}$  1.4737.

For purification from admixed ketone the alcohol was treated with Girard reagent ("P") [23]. We heated 43 g of alcohol with 10 g of reagent and 8.37 g of acetic acid in 120 ml of anhydrous alcohol for 1.5 hours on a water bath. After cooling, the solution was poured into ice water which contained 6.66 g of soda (an amount needed to neutralize 90% of the acetic acid taken). The reaction mixture remained acid to bromthymol blue. The purified alcohol was extracted with ether. The ether extract was washed with a solution of sodium bicarbonate, dried with ignited  $\text{MgSO}_4$ , and fractionated first at ordinary pressure (distillation of the ether) and then in a vacuum.

We thus obtained 30.5 g of purified acetylenic alcohol (yield 56.5% on the starting ketone) with the constants given in Table 1.

TABLE 2

Constants of the Starting Telomers

Substance	B.p. (pressure in mm)	$d_4^{20}$	$n_D^{20}$
$\begin{array}{c} \text{CH}_3-\text{C}=\text{CH}-\text{CH}_2-\text{CH}_2-\text{C}=\text{CH}-\text{CH}_2\text{Cl} \\   \qquad \qquad \qquad   \\ \text{CH}_3 \qquad \qquad \qquad \text{CH}_3 \end{array}$	54-78° (2)	0.9357	1.4380
$\begin{array}{c} \text{CH}_3-\text{CH}=\text{CH}-\text{CH}-\text{CH}_2-\text{C}=\text{CH}-\text{CH}_2\text{Cl} \\   \qquad \qquad \qquad   \\ \text{CH}_3 \qquad \qquad \qquad \text{CH}_3 \end{array}$	84-87 (10)	0.9132	1.4728
$\begin{array}{c} \text{CH}_3-\text{CH}=\text{CH}-\text{CH}-\text{CH}_2-\text{C}=\text{CH}-\text{CH}_2\text{Cl} \\   \qquad \qquad \qquad   \\ \text{CH}_3 \qquad \qquad \text{Cl} \end{array}$	91-93 (10)	1.0382	1.4866

TABLE 3

Constants of the Diene Ketones

Substance	B.p. (10 mm)	$d_4^{20}$	$n_D^{20}$	Yield, %
$\begin{array}{c} \text{CH}_3-\text{C}=\text{CH}-\text{CH}_2-\text{CH}_2-\text{C}=\text{CH}-\text{CH}_2-\text{CH}_2-\text{CO}-\text{CH}_3 \\   \qquad \qquad \qquad   \\ \text{CH}_3 \qquad \qquad \qquad \text{CH}_3 \end{array}$	123-125°	0.8698	1.4670	57
$\begin{array}{c} \text{CH}_3-\text{CH}=\text{CH}-\text{CH}-\text{CH}_2-\text{C}=\text{CH}-\text{CH}_2-\text{CH}_2-\text{CO}-\text{CH}_3 \\   \qquad \qquad \qquad   \\ \text{CH}_3 \qquad \qquad \qquad \text{CH}_3 \end{array}$	118-121	0.8627	1.4620	59
$\begin{array}{c} \text{CH}_3-\text{CH}=\text{CH}-\text{CH}-\text{CH}_2-\text{C}=\text{CH}-\text{CH}_2-\text{CH}_2-\text{CO}-\text{CH}_3 \\   \qquad \qquad \qquad   \\ \text{CH}_3 \qquad \qquad \text{Cl} \end{array}$	129-132	0.9732	1.4738	45

TABLE 4

Analytical Data for the Alcohols

Substance	Found %				Calculated %			
	C	H	Cl	acetylenic alcohol	C	H	Cl	acetylenic alcohol
I	81.67, 81.79	11.12, 11.08	— —	98.8, 97.2	81.76	10.98	—	100
II	81.96, 81.84	11.08, 11.14	— —	98.8, 97.2	81.76	10.98	—	100
III	69.96, 70.01	8.91, 8.86	14.56, 14.73	96.9, 97.2	69.84	8.79	14.73	100
IV	80.97, 80.90	11.50, 11.62	— —	—	81.02	11.78	—	—
V	81.10, 80.92	11.58, 11.47	— —	—	81.02	11.78	—	—
VI	69.20, 69.13	9.62, 9.67	14.53, 14.55	—	69.26	9.55	14.60	—

The analytical data for all the alcohols are given in Table 4. The content of compound with a terminal acetylene grouping was determined by the usual method [21].

The acetylenic alcohols were hydrogenated in methyl alcohol in the presence of 0.2-0.3 g of Pd/CaCO<sub>3</sub> (containing 0.012 g Pd per g of catalyst) to the absorption of 1 mole of hydrogen per 1 mole of substance. At the end of the hydrogenation the catalyst was filtered off, and the alcohol was distilled on a column with a low vacuum on a water bath. The residue was distilled in a vacuum at 10 mm. The content of primary alcohol was determined by the method of phthalate formation [22]. It did not exceed 2-3.5%. The content of acetylenic alcohol: also did not exceed 2-3%.

Nerolidol was converted to farnesol as follows. By the action of phosphorus tribromide in dry pyridine it was converted to the bromide. The bromide was transformed into farnesol acetate by the action of anhydrous potassium acetate in dimethylformamide. The acetate was saponified with 10% KOH. Farnesol was purified through the phthalate. Its constants are given in Table 1.

#### SUMMARY

1. We have showed the possibility of synthesis of sesquiterpene alcohols, their isomers and analogs based on products of telomerization of diene hydrocarbons with their hydrochlorides.

2. We have described for the first time the diene alcohols 3, 7, 9-trimethyl-6,10-dodecadien-1-yn-3-ol and 7-chloro-3,9-dimethyl-6,10-dodecadien-1-yn-3-ol, and the alcohols of the triene series 3,7,9-trimethyl-1,6,10-dodecadien-3-ol and 7-chloro-3,9-dimethyl-1,6,10-dodecatrien-3-ol.

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## THE REACTIONS OF MERCURY SALTS WITH SECONDARY-TERTIARY $\alpha$ -GLYCOLS OF THE ACETYLENE SERIES

### III.\* 5,5-DIMETHYL-1,2-DIPHENYL-3-HEXYN-1,2-DIOL AND MERCURIC CHLORIDE AND SULFATE

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It was shown earlier that under the action of an alcoholic solution of mercuric chloride on secondary-tertiary acetylenic  $\alpha$ -glycols (1,2,4-triphenyl-3-butyne-1,2-diol and 3-methyl-5-phenyl-4-pentyne-2,3-diol), with heating there were formed good yields of substituted furans [1, 2].

Further, in the case of 2-methyl-1,4-diphenyl-3-butyne-1,2-diol it was shown that under milder conditions it was possible to isolate an intermediate reaction product, a substituted  $\beta$ -chloromercurifuran. Then a mechanism was suggested for conversion of acetylenic  $\alpha$ -glycols to substituted furans.

The formation of  $\beta$ -chloromercurifurans is especially valuable in the reaction of primary-tertiary  $\alpha$ -glycols of the acetylenic series with mercury salts since in this case we can obtain  $\beta$ -chloromercurifurans which are not substituted in the  $\alpha$ -position—compounds hard to obtain. It was also shown that under the action of mercuric sulfate acetylenic  $\alpha$ -glycols could be converted into substituted furans [4, 5].

In order to determine whether the reaction of mercury salts with acetylenic  $\alpha$ -glycols was a general method for obtaining furans and their  $\beta$ -chloromercuriderivatives we studied the action of mercuric chloride and sulfate on sym-diphenyl-tert-butylacetylenyl-ethylene glycol (5,5-dimethyl-1,2-diphenyl-3-hexyne-1,2-diol). All the glycols of this type studied earlier contained a residue of phenylacetylene; in this case the acetylene hydrogen of the glycol was replaced by a tert-butyl group.

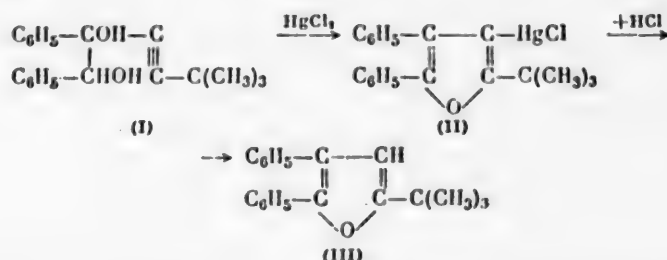
Sym-diphenyl-tert-butylacetylenyl-ethylene glycol (I) was synthesized by the process of Zh. I. Iotsich, starting from benzoin and tert-butylacetylene. By the action of mercuric chloride on this glycol, as in the case of the glycols studied earlier, a good yield of 2,3-diphenyl-5-tert-butylfuran (III) was obtained. As before, the yield of furan did not depend on the amount of mercury salt used in the reaction (within the limits from 1 to 0.25 mole of mercuric chloride per 1 mole of glycol).

Considering the suggested mechanism of formation of substituted furans [3], we believed it to be expedient in preparing the furans to add a small amount of acid for the purpose of hastening and making more complete the decomposition of the intermediate reaction product, the  $\beta$ -chloromercurifuran. This was especially important when using a small amount of salt with respect to the glycol, since under rather mild reaction conditions some unchanged mercuriated furan might remain.

The mercuriated furan 2,3-diphenyl-2-tert-butyl-4-mercurifuran (II) was isolated by pouring together equimolecular alcoholic solutions of the glycol and mercuric chloride. In this case colorless crystals of the

\* Communication I: Zhur, Obshchei Khim., 28, 3227 (1958); Communication II: Zhur Obshchei Khim., 29, 81 (1959).

$\beta$ -chloromercurifuran (II) precipitated quite rapidly, though more slowly than in the previous cases; when they were boiled with alcohol with the addition of a small amount of hydrochloric acid they decomposed, forming the substituted furan (III).



The slower reaction of glycol (I) with mercuric chloride with formation of the  $\beta$ -chloromercurifuran (II) compared to the glycols previously studied can evidently be explained by special hindrance of the tert-butyl group.

## EXPERIMENTAL

### Preparation of 5,5-Dimethyl-1,2-diphenyl-3-hexyn-1,2-diol (I)

To a freshly prepared solution in ether of tert-butyl-acetylenylmagnesium bromide prepared as usual from 14 g of magnesium was added a solution of 25 g of benzoin (half quantity) in 500 ml of anhydrous benzene. The remaining 25 g of benzoin was added to the reaction in the form of a dry, finely ground powder. The mixture was heated for two hours with stirring at 40°. After decomposition of the magnesium organic complex with dilute hydrochloric acid and drying of the separated benzene layer, the solvent was distilled off. The residue quickly crystallized. We obtained 52 g of crude product and from it, after two crystallizations from a mixture of benzene and ligroin (2:3), 40 g (58%) of pure substance with m. p. 132-133°.

From the mother liquor we isolated 3 g of a substance with m. p. 93-95°, which, to judge from the analysis, was probably an isomer of the glycol with m. p. 132-133°. The presence of two isomers was caused by two asymmetric carbon atoms in the acetylene  $\alpha$ -glycol (I). Preparation of acetylenic  $\alpha$ -glycols in two modifications was noted [2] for 3-methyl-5-phenyl-4-pentyn-2,3-diol [3], and also for 3,5-dimethyl-1-hexyn-3,4-diol [6]. In view of the small amount of the substance with m. p. 93-95°, it was not investigated further.

Analysis of the glycol with m. p. 132-133°:

Found %: C 81.75, 81.48; H 7.58, 7.60; OH 11.22. M 283.1.  $\text{C}_{20}\text{H}_{22}\text{O}_2$ . Calculated %: C 81.63; H 7.49; OH 11.56. M 294.

Analysis of the glycol with m. p. 93-95°:

Found %: C 81.72, 81.48; H 7.80, 7.51; OH 11.16. M 279.  $\text{C}_{20}\text{H}_{22}\text{O}_2$ . Calculated %: C 81.63; H 7.49; OH 11.56. M 294.

### Action of Mercuric Chloride on 5,5-Dimethyl-1,2-diphenyl-3-hexyn-1,2-diol\*

**Experiment 1.** We dissolved 5 g of glycol (m. p. 132-133°) and 5.2 g of mercuric chloride (molar ratio) separately in a total volume of 50 ml of alcohol. When the solutions were poured together, a crystalline precipitate began to appear after several minutes, and the entire mass quickly solidified. After boiling for one hour with alcohol, the precipitate dissolved. The solution was poured into 500 ml of water and was extracted with benzene. After drying with sodium sulfate and distillation of the benzene the residue crystallized. We obtained 3.2 g of substance with m. p. 68-69° (from ligroin). The substance was easily soluble in ether and acetone, poorly so in methanol and ethanol, decolorized a chloroform solution of bromine and a water solution of potassium permanganate when heated; reactions for hydroxyl and carbonyl groups were negative.

\* In distinction from the previous experiments [3, 4] the reaction of the glycol with mercuric chloride was carried out without stirring.

Found %: C 36.89, 86.94; H 7.40, 7.35, M 269.8,  $C_{20}H_{19}O$ . Calculated %: C 86.96; H 7.25, M 276.

On the basis of the analytical data and the properties of the substance with m. p. 68-69° it must be considered to be the 2,3-diphenyl-5-tert-butylfuran (II) described in the literature [7]. Yield 68.2%.

Experiment 2. Considering the mechanism of formation of the substituted furans [3], we repeated experiment 1 with the same amount of starting substances, but with the addition of 1 ml of concentrated hydrochloric acid for more rapid decomposition of the precipitate which first precipitated. We obtained 3.5 g (74.6%) of the substituted furan with m. p. 68-69°.

Experiment 3. To show the effect of molar ratio of glycol and mercuric chloride on the yield of furan we carried out experiments starting with 5 g of glycol and 1.3 g of mercuric chloride. We obtained 3.2 g (68.2%) of substituted furan (III).

Experiment 4. To show the nature of the intermediate product obtained in the reaction of the acetylene  $\alpha$ -glycol with mercuric chloride, 5 g of the glycol and 5.2 g of mercuric chloride were dissolved in a total volume of 50 ml of alcohol and poured together. The crystalline precipitate after standing for eight hours at room temperature was filtered off and washed with 30 ml of cold alcohol. We obtained 7.5 g of colorless crystals with m. p. 193-199° (from alcohol).

Found %: C 47.21, 47.08; H 3.94, 3.93; Hg 39.15, 39.12; Cl 6.93, 6.88,  $C_{20}H_{19}OClHg$ . Calculated %: C 46.96; H 3.72; Hg 39.25; Cl 6.95.

When this substance was boiled with alcohol with the addition of hydrochloric acid it formed 2,3-diphenyl-5-tert-butylfuran. It did not contain hydroxyl or carbonyl groups. Yield 86.3%, calculated on the assumption that the substance is 2,3-diphenyl-5-tert-butyl-4-chloromercurifuran (II).

#### Action of Mercuric Sulfate on 5,5-Dimethyl-1,2-diphenyl-3-hexyn-1,2-diol

Five g of glycol, 2.5 g of mercuric sulfate, 50 ml of alcohol, and 1 ml of concentrated sulfuric acid were heated for one hour in boiling alcohol. A considerable part of the mercuric sulfate did not dissolve. After cooling, the precipitate was filtered and washed with benzene. The alcoholic filtrate was diluted with 300 ml of water and extracted with benzene. The combined benzene solutions were washed with water and dried with sodium sulfate. After distillation of the benzene we obtained 3.1 g (66.2%) of the substituted furan (III) with m. p. 68-69°.

Hence, by the action of mercuric sulfate on 5,5-dimethyl-1,2-diphenyl-3-hexyn-1,2-diol we obtained 2,3-diphenyl-5-tert-butylfuran.

#### SUMMARY

1. We have synthesized the undescribed sym-diphenyl-tert-butylacetylenylethylene glycol (5,5-dimethyl-1,2-diphenyl-3-hexyn-1,2-diol) and studied its reactions under the influence of mercuric chloride and sulfate.

2. We have showed that this glycol, like the previously studied secondary-tertiary  $\alpha$ -glycols with phenylacetylenyl residues, easily forms a substituted furan, 2,3-diphenyl-5-tert-butylfuran, in the presence of mercury salts.

3. We have isolated the previously undescribed intermediate product of the reaction of the glycol with mercuric chloride, the substituted  $\beta$ -chloromercurifuran, 2,3-diphenyl-5-tert-butyl-4-chloromercurifuran. We have showed that when this compound is heated with hydrochloric acid it is transformed into the substituted furan which confirms the suggested scheme for formation of furans from secondary-tertiary  $\alpha$ -glycols of the acetylene series.

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## HETEROCYCLIC COMPOUNDS

### SYNTHESIS OF THE BENZOATES OF

#### 1-ALKENYL-2,5-DIMETHYL-4-VINYL-PIPERIDOLS

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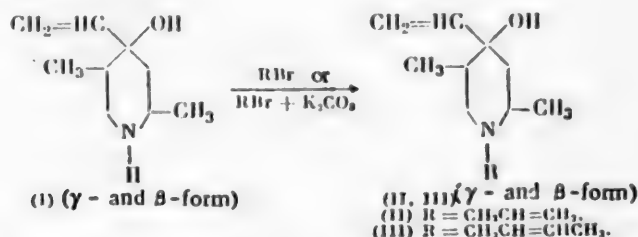
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November, 1960

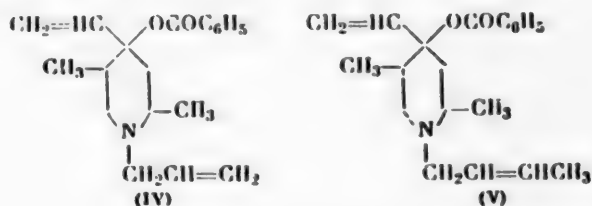
Original article submitted December 14, 1959

In a previous communication [1] the esters of the 1-alkenyl-2,5-dimethyl-4-ethynyl-4-piperidols have been described; several of them were found to have a high anesthetic activity. The present work deals with the synthesis of 1-alkenyl-2,5-dimethyl-4-vinyl-4-piperidols and the benzoates of their  $\gamma$ -isomers.

The 1-alkenyl-2,5-dimethyl-4-vinyl-4-piperidols (II) and (III) are obtained in high yields (78-87%) from the individual  $\gamma$ - and  $\beta$ -isomers of 2,5-dimethyl-4-vinyl-4-piperidol (I) [2] by the action of the corresponding halgeon derivatives of allylic type, either in benzene solution [3], or in 1-butanol or ethanol solution in the presence of potassium carbonate [4, 5].



For the purpose of pharmacological studies, the benzoates (IV) and (V) were synthesized by the esterification of the  $\gamma$ -isomers of 1-allyl- and 1-crotyl-2,5-dimethyl-4-vinyl-4-piperidols (II) and (III), respectively, with benzoyl chloride in dry pyridine.



### EXPERIMENTAL

1-Allyl-2,5-dimethyl-4-vinyl-4-piperidol (II). a) To a solution of the  $\gamma$ -form of 2,5-dimethyl-4-vinyl-4-piperidol (m. p. 125-126°) [6] (10 g) in 80 ml of dry benzene heated to 90° on a water bath was added, dropwise

and with stirring, a solution of 4.23 g of allyl bromide in 10 ml of anhydrous benzene; the mixture was heated at 90-95° for 3 hr and left to stand overnight. On the next day, heating was resumed for a further period of 5 hr. The hydrochloride of the original piperidol, which separated out, was then filtered and washed, and the solution of the product in benzene was treated with 15 ml of water (to remove the soluble hydrobromide). After drying over anhydrous potassium carbonate, the benzene was distilled off, and the crystalline residue was recrystallized from benzene (b. p. 60-80°). Yield: 5.37 g of the  $\gamma$ -form of 1-allyl-2,5-dimethyl-4-vinyl-4-piperidol (II), m. p. 61-62° (86% based on the piperidol which reacted).

Found %: N 7.47, 7.57.  $C_{12}H_{21}ON$ . Calculated %: N 7.17.

The hydrochloride of the  $\gamma$ -form of the piperidol (II) was obtained by adding an ethereal solution of dry hydrogen chloride to an alcoholic solution of the piperidol and recrystallizing the product from acetone. Yield: 0.38 g of the hydrochloride, m. p. 146-147°, from 0.4 g of the piperidol.

Found %: N 6.05, 6.03; Cl 14.80, 15.10.  $C_{12}H_{22}ONCl$ . Calculated %: N 6.04; Cl 15.30.

b) To a mixture of 19 g of the  $\gamma$ -form of 2,5-dimethyl-4-vinyl-4-piperidol (m. p. 125-126°) in 50 ml of dry 1-butanol and 17.7 g of powdered anhydrous potassium carbonate was added, at 80°, dropwise and with efficient stirring, a solution of 8.5 g of allyl bromide in 10 ml of dry 1-butanol. The reaction mixture was heated at 70-75° for 7 hr. On the next day, the residue (potassium bromide and excess of potassium carbonate) was filtered off and washed. The butanol solution was distilled to dryness on a water bath under reduced pressure (water pump). Recrystallization from benzene of the residue thus obtained gave 9.75 g (78% yield based on the starting piperidol) of the  $\gamma$ -form of 1-allyl-2,5-dimethyl-4-vinyl-4-piperidol (II), m. p. 61-62°.

c) A mixture of 15.5 g of the  $\beta$ -form of 2,5-dimethyl-4-vinyl-4-piperidol (m. p. 82-83°) [2] and 7.5 g of allyl bromide in 80 ml of dry benzene was heated at 80-85°, with stirring for 5 hr. On the next day, the hydrochloride of the original piperidol (obtained as a thick mass) was removed and washed with benzene; the benzene solution of the reaction product was treated with 20 ml of water. It was then dried over anhydrous potassium carbonate, the solvent distilled off, and the crystalline residue recrystallized from benzene to give 5.5 g of the  $\beta$ -form of 1-allyl-2,5-dimethyl-4-vinyl-4-piperidol (II), m. p. 51-52°.

Found %: N 7.21, 7.38.  $C_{12}H_{21}ON$ . Calculated %: N 7.17.

The hydrochloride of the  $\beta$ -form of the piperidol (II) melts at 166-167° (from alcohol). Yield: 0.19 g from 0.20 g of the piperidol.

Found %: Cl 15.12, 15.21.  $C_{12}H_{22}ONCl$ . Calculated %: Cl 15.30.

1-Crotyl-2,5-dimethyl-4-vinyl-4-piperidol (III). a) To a solution of 20 g of the  $\gamma$ -form of 2,5-dimethyl-4-vinyl-4-piperidol (m. p. 125-126°) in 280 ml of dry benzene at 60° was added, dropwise and with stirring, a solution of 10.6 g of freshly distilled primary crotyl bromide (b. p. 103° at 704 mm,  $n_D^{20}$  1.4805) [7] in 10 ml of dry benzene. The addition took 20 min; the mixture was then heated at 55-60° for 5 hr. On the next day the hydrochloride of the original piperidol, which separated out, was filtered off and washed with benzene and dry ether. The benzene and ether were distilled off and the residue thus obtained was recrystallized from benzene (b. p. 100-120°), giving 11.7 g of the  $\gamma$ -form of 1-crotyl-2,5-dimethyl-4-vinyl-4-piperidol (III), m. p. 86-87° (87.3% yield based on the piperidol which reacted).

Found %: N 6.69, 6.84.  $C_{13}H_{23}ON$ . Calculated %: N 6.69.

The hydrochloride of the  $\gamma$ -form of piperidol (III) was obtained by adding a solution of dry hydrogen chloride in ether to an alcoholic solution of the piperidol. Yield, from 0.50 g of the starting material: 0.47 g of the hydrochloride, m. p. 187-188° (from a mixture of alcohol and ether).

Found %: Cl 14.22, 14.44.  $C_{13}H_{24}ONCl$ . Calculated %: Cl 14.43.

b) To a mixture of 5 g of the  $\beta$ -form of 2,5-dimethyl-4-vinyl-4-piperidol (m. p. 82-83°) and 8.85 g of anhydrous potassium carbonate in 20 ml of absolute alcohol at 50° was added, with vigorous stirring, 4.75 g of freshly distilled primary crotyl bromide (b. p. 78° at 90 mm,  $n_D^{20}$  1.4805); then the mixture was heated at 55-60° for 6.5 hr. After cooling, the residue (potassium bromide and excess of potassium carbonate) was filtered off and washed with dry ether. Following the removal of ether and alcohol by distillation, the crystalline residue was recrystallized from petroleum ether (b. p. 50-69°). Yield: 5.5 g (82.1%) of the  $\beta$ -form of 1-crotyl-2,5-dimethyl-4-vinyl-4-piperidol (III), m. p. 60-61°.

Found %: N 6.62, 6.68,  $C_{13}H_{23}ON$ . Calculated %: N 6.69.

The hydrochloride of the  $\beta$ -form of the piperidol (III) was obtained by the addition of a solution of dry hydrogen chloride in ether to an alcoholic solution of the piperidol until the mixture was acid to Congo red, followed by precipitation of the hydrochloride thus formed by treatment with absolute ether. Yield, from 0.5 g of the piperidol: 0.53 g of the hydrochloride, m. p. 144-146° (from alcohol-ether mixture).

Found %: N 5.68, 5.80; Cl 14.46, 14.28.  $C_{13}H_{24}ONCl$ . Calculated %: N 5.69; Cl 14.43.

Benzoate of 1-allyl-2,5-dimethyl-4-vinyl-4-piperidol (IV). A solution of 1.95 g of the  $\gamma$ -form of 1-allyl-2,5-dimethyl-4-vinyl-4-piperidol (m. p. 61-62°) in 4 ml of dry pyridine was treated with 4.3 g of benzoyl chloride, and the mixture was heated on a glycerol bath at 100-105° for 6 hr. On the next day the product was diluted with dry ether, and the dark brown precipitate which separated out was filtered off and recrystallized, first from a mixture of acetone and benzene, and then from acetone. Yield: 1.87 g (62.5%) of the hydrochloride of the benzoate of 1-allyl-2,5-dimethyl-4-vinyl-4-piperidol ( $\gamma$ -form) (IV), obtained as fine clusters of needle crystals, m. p. 155-157°.

Found %: N 4.16, 4.05; Cl 10.64, 10.60.  $C_{15}H_{26}O_2NCl$ . Calculated %: N 4.17; Cl 10.55.

Benzoate of 1-crotyl-2,5-dimethyl-4-vinyl-4-piperidol (V). A mixture of the  $\gamma$ -form of 1-crotyl-2,5-dimethyl-4-vinyl-4-piperidol (m. p. 86-87°) (2.09 g) and benzoyl chloride (4.2 g) in 5 ml of dry pyridine was heated at 100-105° for 6 hr, then cooled and diluted with dry ether. The precipitate thus obtained was crystallized successively from benzene and acetone. Yield: 1.88 g (60%) of the hydrochloride of the benzoate of 1-crotyl-2,5-dimethyl-4-vinyl-4-piperidol ( $\gamma$ -form) (V), obtained as white needle crystals, m. p. 154-156°.

Found %: N 4.03, 3.89; Cl 10.03, 9.92.  $C_{20}H_{28}O_2NCl$ . Calculated %: N 4.00; Cl 10.13.

#### SUMMARY

1. The  $\gamma$ - and  $\beta$ -isomers of 1-allyl- and 1-crotyl-2,5-dimethyl-4-vinyl-4-piperidols were synthesized in high yields (78-87%) by alkenylation of the corresponding  $\gamma$ - and  $\beta$ -isomers of 2,5-dimethyl-4-vinyl-4-piperidol with allyl bromide or crotyl bromide, either in benzene solution or in 1-butanol and ethanol in the presence of potassium carbonate.

2. The benzoates of the  $\gamma$ -isomers of 1-allyl- and 1-crotyl-2,5-dimethyl-4-vinyl-4-piperidols thus obtained were prepared by their esterification with benzoyl chloride.

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## ESTERS OF DI-n-PROPYLARSINOUS ACID

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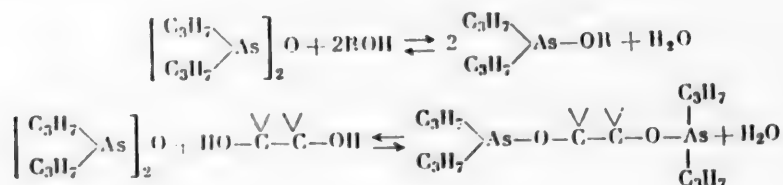
The present work is a further development in our investigations of esters of acids of trivalent arsenic [1].

No one has studied the esters of di-n-propylarsinous acid. We synthesized these esters by the two following methods:

a) by the reaction of di-n-propyldoarsine with sodium alcoholates



b) by the reaction of bis-di-n-propylarsine oxide with appropriate alcohols and glycols at an elevated temperature.



The second method gave the best yields. The reaction of di-n-propyldoarsine with sodium alcoholates was complex and did not proceed to completion, and therefore the esters of di-n-propylarsinous acid obtained were impure.

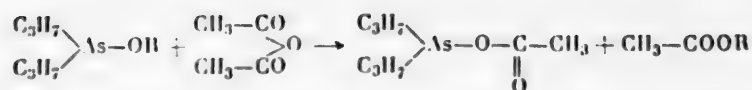
As a result of the experiments, we obtained the esters of di-n-propylarsinous acid given in the table.

The alkyl esters of di-n-propylarsinous acid we isolated were mobile, colorless liquids. They dissolved readily in many organic solvents and were hydrolyzed comparatively readily. Hydrolysis of the esters formed bis-di-propylarsine oxide.

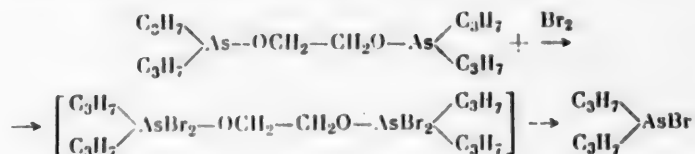


The esters of di-n-propylarsinous acid reacted with methyl iodide or benzyl bromide in a sealed tube over a long period to form crystalline addition products, which we did not study in detail. The esters also reacted with cuprous salts with the evolution of heat and the formation of a sirupy product.

We then established that when a mixture of acetic anhydride and an ester of di-n-propylarsinous acids was heated a reaction occurred to form the corresponding alkyl ester of acetic acid and the acetyl derivative of di-n-propylarsinous acid.



It is interesting to note that the bromination of the ethylene ester of di-n-propylarsinous acid resulted in the addition of exactly two molecules of bromine to one molecule of ester. The addition product did not crystallize. Its hydrolysis yielded di-n-propylbromoarsine.



We were unable to isolate other individual substances.

#### EXPERIMENTAL

Preparation of bis-di-n-propylarsine oxide. A mixture of 96.6 g of di-n-propyliodoarsine and a solution of 31.4 g of potassium hydroxide in 72 ml of water was shaken repeatedly in a separatory funnel for 3 hr. The oxide layer was then separated, washed twice with water, dried over calcium chloride, and vacuum distilled in a stream of nitrogen. The oxide yield was 93.4%.

B. p. 122-125° (4 mm),  $d_4^{20}$  1.1750,  $n_D^{20}$  1.4985,  $M_R$  84.43,  $AR_{As}$ ... 11.20. Found %: As 44.22.  $C_{12}H_{28}OAs_2$ . Calculated %: As 44.30.

Bis-di-n-propylarsine oxide was a colorless liquid which was readily oxidized in air.

Preparation of ethyl di-n-propylarsinite. Into a three-necked flask with a stirrer, a reflux condenser, and dropping funnel was placed the sodium ethylate from 1.2 g of sodium in 100 ml of absolute ether; a solution of 15 g of di-n-propyliodoarsine in 30 ml of dry ether was added dropwise to this mixture with stirring. The reaction mixture was then stirred first at room temperature and then on a water bath for 1 hr and left overnight. The next day, after removal of the solvent, the residual mass was vacuum distilled with a pear fractionating column, 12 cm high. After two distillations the substance had the following constants.

B. p. 74.5-75.5 (20 mm),  $d_4^{20}$  1.0718,  $n_D^{20}$  1.4621,  $M_R$  52.88,  $AR_{As}$ ... 11.00. Found %: As 36.36.  $C_8H_{19}OAs$ . Calculated %: As 36.33.

The ester isolated was a colorless, refracting liquid.

Preparation of n-propyl di-n-propylarsinite. Into an Arbuzov flask were placed 10 g of bis-di-n-propylarsine oxide and 9 ml of anhydrous n-propanol. The side-tube of the flask was connected to a small holder with baked copper sulfate. The flask was then placed in a position for refluxing and the mixture heated at 80° for 2 hr. The holder was removed and the mixture vacuum distilled. Two vacuum distillations gave a 76.1% yield of a fraction with the following constants:

B. p. 83-84° (13 mm),  $d_4^{20}$  1.0469,  $n_D^{20}$  1.4615,  $M_R$  57.75,  $AR_{As}$ ... 11.25. Found %: As 33.95.  $C_9H_{21}OAs$ . Calculated %: As 34.02.

All the other esters of di-n-propylarsinous acid were obtained analogously, with the difference that in the case of higher alcohols the mixture was heated under slightly reduced pressure without water-abstracting reagents. Some data on them are given in the table.

Preparation of phenyl di-n-propylarsinite. A solution of 5.8 g of di-n-propylchloroarsine in 30 ml of ether was added dropwise with stirring to a mixture of 3.43 g of sodium phenolate and 50 ml of diethyl ether. The contents of the flask were then heated on a water bath for 2 hr. The next day the solvent was removed and the residual mass vacuum distilled. Redistillation yielded 2.5 g (33.4%) of a colorless liquid.

B. p. 136-137° (11 mm),  $d_4^{20}$  1.1559,  $n_D^{20}$  1.5332,  $M_R$  68.27,  $AR_{As}$ ... 11.51. Found %: As 29.26.  $C_{12}H_{19}OAs$ . Calculated %: As 29.47.

Esters of Di-n-Propylarsinous Acid

Sample No.	Ester formula	B.p. (pressure in mm)	$d_4^{20}$	$n_D^{20}$	MR <sub>D</sub>	AR <sub>As</sub> <sup>...</sup>	% As		Yield, %
							found	calcd.	
1	(C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> AsOC <sub>2</sub> H <sub>5</sub>	72° (18)	1.0718	1.4621	52.98	11.00	36.36	36.33	20.5
2	(C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> AsOC <sub>3</sub> H <sub>7</sub>	82 (13)	1.0468	1.4615	57.75	11.25	33.95	34.02	76.2
3	(C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> AsOC <sub>4</sub> H <sub>9</sub> n	101—102 (14)	1.0327	1.4618	62.18	11.06	32.14	31.98	77.3
4	(C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> AsOC <sub>4</sub> H <sub>9</sub> -iso	85—86 (9)	1.0266	1.4606	62.48	11.35	31.86	31.98	83.6
5	(C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> AsOC <sub>6</sub> H <sub>13</sub> n	130—131 (16)	1.0068	1.4625	71.67	11.31	28.52	28.56	57.6
6	(C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> AsOC <sub>6</sub> H <sub>13</sub> n	143—144 (5)	0.9779	1.4650	85.74	11.59	24.60	24.80	89.0
7	(C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> AsOC <sub>8</sub> H <sub>17</sub> n	136—137 (11)	1.1559	1.5352	68.27	11.51	29.26	29.47	33.3
8	(C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> AsOC <sub>8</sub> H <sub>17</sub> -1/2	140—142 (2.5)	1.1760	1.4922	94.34	11.00	39.69	39.65	82.1
9	(C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> As—O—C(=O)—CH <sub>3</sub>	101 (17)	1.1408	1.4680	53.54	11.64	33.57	34.02	89.6

Reaction of n-hexyl di-n-propylarsinite with acetic anhydride. Into an Arbuzov flask set up for distillation were placed 6.7 g of n-hexyl di-n-propylarsinite and 4.0 g of acetic anhydride. No temperature changes were observed when the reagents were mixed. The mixture was heated for 3 hr until the odor of acetate appeared. Distillation yielded the following fractions: 1st with b. p. 65–72° (18 mm) and 2nd with b. p. 101° (17 mm).

Redistillation of the first fraction yielded a substance with b. p. 169–169.5,  $n_D^{20}$  1.14100, which corresponds to n-hexyl acetate.

We obtained 5.0 g (89.6%) of the second fraction.

B. p. 101° (17 mm),  $d_4^{20}$  1.1408,  $n_D^{20}$  1.4680, MR<sub>D</sub> 53.54, AR<sub>As</sub>... 11.64. Found %: As 33.30, C<sub>8</sub>H<sub>17</sub>O<sub>2</sub>As. Calculated %: As 33.65.

The acetyl derivative of di-n-propylarsinous acid was a colorless liquid, which was readily hydrolyzed.

Bromination of ethylene di-n-propylarsinite. With good external cooling, 5 ml of bromine in 50 ml of carbon tetrachloride was added dropwise to 15.8 g of ethylene di-n-propylarsinite in 50 ml of carbon tetrachloride. A large amount of heat was liberated during the reaction. The solution was pale yellow when the calculated amount of bromine had been added. The next day the solvent was removed by filtration in vacuum, and the residual thick mass did not crystallize on long standing. Pyrolysis of this mass yielded a fraction with b. p. 199–209°. Redistillation of this fraction yielded a substance with b. p. 79° (11 mm) and  $n_D^{20}$  1.5515.

Found %: As 30.89, C<sub>6</sub>H<sub>14</sub>AsBr. Calculated %: As 31.04.

Synthesis from bis-di-n-propylarsine oxide and hydrogen bromide yielded di-n-propylbromoarsine, which boiled at 79° (11 mm) and had  $n_D^{20}$  1.5301.

Thus, we were able to isolate only di-n-propylbromoarsine as a result of pyrolysis of the bromination product of ethylene di-n-propylarsinite. We were unable to isolate other individual substances.

## SUMMARY

1. The ethyl, n-propyl, n-butyl, isobutyl, n-hexyl, n-nonyl, phenyl, and ethylene esters of di-n-propylarsinous acid were prepared and studied for the first time.

2. It was established that alkyl esters of di-n-propylarsinous acid react with alkyl halides to form onium compounds.

3. The esters isolated reacted with acetic anhydride to form the corresponding acetate and the acetyl derivative of di-n-propylarsinous acid.

4. It was established that in the bromination of ethylene di-n-propylarsinite, two molecules of bromine are added to one molecule of ester. From the pyrolysis products of brominated ethylene di-n-propylarsinite we were able to isolate di-n-propylbromoarsine.

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## ORGANOBORON COMPOUNDS

### LXII.\* SYNTHESIS OF ORGANOBOROSILICON COMPOUNDS

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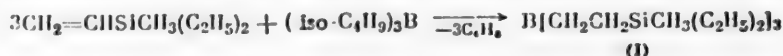
Translated from *Zhurnal Obshchei Khimii*, Vol. 30, No. 11, pp. 3615-3619,

November, 1960

Original article submitted December 26, 1959

Shegoleva and one of us [1] found that trisobutylboron reacts with allyltrimethylsilane or allyltrichlorosilane with heating to form tri-(3-trimethylsilylpropyl)-boron and tri-(3-trichlorosilylpropyl)-boron, respectively.

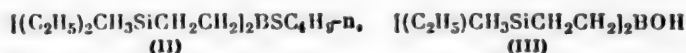
To prepare organoborosilicon compounds containing boron and silicon atoms at neighboring carbon atoms and study their chemical properties, we synthesized this type of compounds by "transalkylation" of trisobutylboron with vinyl derivatives of silicon. Heating a mixture of 1 mole of trisobutylboron and 3 moles of vinylmethyldiethylsilane at 130-140° for 6 hr gave a 63% yield of tri-(2-methyldiethylsilylethyl)-boron (I).



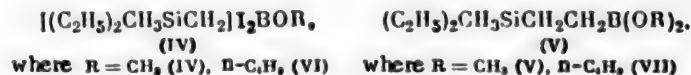
The substance obtained was assigned the given structure on the basis of the data of Brown and Rao [2], who showed that the reaction of trialkylborons and higher olefins forms higher trialkylborons with primary hydrocarbon radicals.

It is interesting that by the action of sodium borohydride and aluminum chloride on vinyltrimethylsilane, Seyferth [3] obtained a mixture of the two possible isomers  $[(\text{CH}_3)_3\text{SiCH}_2\text{CH}_2]_3\text{B}$  and  $[(\text{CH}_3)_3\text{SiCH}(\text{CH}_3)]_3\text{B}$ , from which he was unable to isolate individual compounds.

Like trialkylborons [4], tri-(2-methyldiethylsilylethyl)-boron reacted smoothly with n-butyl mercaptan to form the n-butyl ester of di-(2-methyldiethylsilylethyl)-thioboric acid (II) and methyltriethylsilane.



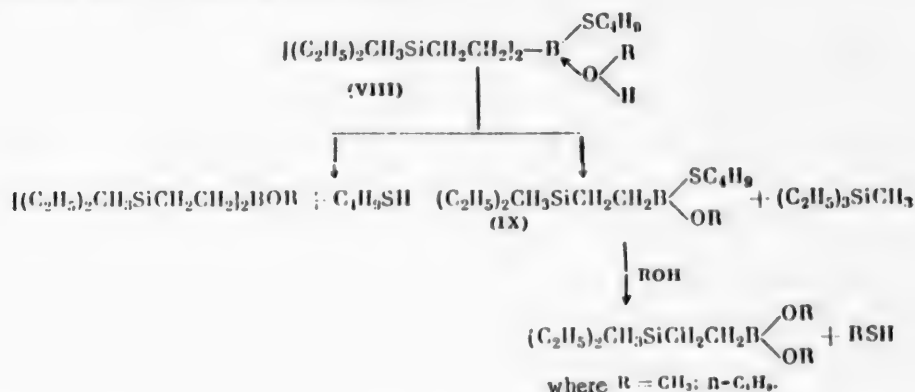
The ester (II) reacted with water in the cold to form di-(2-methyldiethylsilylethyl)-boric acid (III), which could be vacuum distilled, in contrast to dialkylboric acids. The action of methanol on the ester (II) formed not only the expected methyl ester of di-(2-methyldiethylsilylethyl)-boric acid (IV), but also the dimethyl ester of 2-methyldiethylsilylethylboric acid (V).



\* For LIX-LX, see *Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk*, 1880 and 1891 (1960) and for LXI see *Doklady Akad. Nauk SSSR* 133, 119 (1960).

The reaction of the ester (II) with *n*-butanol was analogous and formed the *n*-butyl ester of di-(2-methyldiethylsilylethyl)-boric acid (VI) and the di-*n*-butyl ester of 2-methyldiethylsilylethylboric acid (VII).

It might have been considered that the esters of 2-methyldiethylsilylethylboric acid (V) and (VII) were formed as a result of the action of excess alcohol on the primary reaction products, namely the esters of di-(2-methyldiethylsilylethyl)-boric acid (IV) and (VI). However, it was found that the esters (IV) and (VI) were not converted into esters of 2-methyldiethylsilylethylboric acid by boiling with alcohols. The formation of the esters (V) and (VII) evidently may be explained by the fact that the complexes of esters and alcohols (VIII) formed in the first stage of the reaction not only lose mercaptan with the formation of esters of di-(2-methyldiethylsilylethyl)-boric acid, but also undergo decomposition at the boron-carbon, thereby forming methyltriethylsilane and mixed esters of 2-methyldiethylsilylethylboric acid (IX). The latter are then converted to the esters (V) and (VII) under the action of excess alcohol.



We then studied the reaction between triisobutylboron and vinylmethyldiethoxysilane. Heating the components at 140-145° for 6 hr yielded isobutylene (76% of the theoretical amount) and a complex mixture of products from which tri-(2-methyldiethoxysilylethyl)-boron (X) was isolated by fractional distillation.



The reaction between triisobutylboron and vinylmethyldichlorosilane was also complex and gave a 25% yield of tri-(2-methyldichlorosilylethyl)-boron (XI).

## EXPERIMENTAL

1. Vinylmethyldiethylsilane. This compound was obtained by the method used for synthesizing vinyltriethylsilane [5]. A solution of 100 g of vinylmethyldichlorosilane in 300 ml of ether was added with stirring to the Grignard reagent from 36 g of magnesium, 164 g of ethyl bromide, and 600 ml of ether. When all the silane had been added, the mixture was boiled for 6 hr and then decomposed with saturated ammonium chloride solution and the ether layer dried with calcium chloride. After removal of the ether, the residue was distilled on a column. The yield was 56 g (62%) and the b. p. was 120-122° at 737 mm.

According to literature data, vinylmethyldiethylsilane obtained by the action of potassium hydroxide on  $\alpha$ -chloroethylmethyldiethylsilane has b. p. 118° at 734 mm [6].

2. Vinylmethyldiethoxysilane. This compound was prepared analogously to vinylmethyldimethoxysilane [7]. A mixture of 16 ml of pyridine and 23 ml (0.5 mole) of anhydrous alcohol was added dropwise with cooling to a mixture of 28.2 g (0.2 mole) of vinylmethyldichlorosilane, 20 ml of isopentane, and 16 ml of dry pyridine, and then the reaction mixture was heated for 30 min, the pyridine hydrochloride precipitate removed by filtration, the solvent distilled from the filtrate, and the residue fractionated. The yield was 9 g (27%) and the b. p. was 51-55° at 34 mm.

According to literature data, vinylmethyldiethoxysilane obtained by the action of methylmagnesium bromide on vinyltriethoxysilane has b. p. 133-134° [8].



3. Tri-(2-methyldiethylsilylethyl)-boron (I). A mixture of 49 g (0.27 mole) of triisobutylboron and 95 g (0.74 mole) of methyldiethylvinylsilane was heated at 130-140° for 6 hr, and then the reaction products were fractionated. The yield was 60.9 g (62.7%).

B. p. 182-184° at 2 mm,  $d_4^{20}$  0.8462,  $n_D^{20}$  1.4632. Found %: C 63.01, 63.00; H 12.95, 12.93.  $C_{21}H_{31}BSi_3$ . Calculated %: C 63.31; H 12.90.

We obtained 32 g (78%) of butylene during the experiment.

4. n-Butyl ester of di-(2-methyldiethylsilylethyl)-thioboric acid (II). A 20-ml sample (0.16 mole) of n-butyl mercaptan was added dropwise with stirring to 65.4 g (0.16) of tri-(2-methyldiethylsilylethyl)-boron, when strong heat evolution was observed. The mixture was boiled for 2 hr, and then the reaction products were fractionated. The yield was 48.7 g (82.8%).

B. p. 163-166° at 0.5 mm,  $d_4^{20}$  0.8767,  $n_D^{20}$  1.4821. Found %: C 59.36, 59.61; H 11.78, 11.86; B 3.60, 3.52.  $C_{18}H_{25}SBSi_2$ . Calculated %: C 60.31; H 12.09; B 3.01.

During the experiment we obtained 19.9 g (94%) of methyltriethylsilane with b. p. 122-128°.

5. Di-(2-methyldiethylsilylethyl)-boric acid (III). The n-butyl ester of di-(2-methyldiethylsilylethyl)-thioboric acid (8.5 g, 0.237 mole) was shaken with water in a separatory funnel. Heat was evolved. The reaction mixture was then extracted with ethyl ether and the ether extract dried with sodium sulfate. The ether and mercaptan were removed by distillation and the residue dried in vacuum to constant weight. The yield was 6.3 g (94%).

B. p. 152-160° at 0.01 mm,  $n_D^{20}$  1.4608,  $d_4^{20}$  0.8813. Found %: C 58.81, 58.89; H 12.17, 11.91.  $C_{14}H_{25}OBSi_2$ . Calculated %: C 58.74; H 12.33.

The substance did not change during vacuum distillation. It was a thick, colorless liquid with the odor of camphor.

6. Methyl ester of di-(2-methyldiethylsilylethyl)-boric acid (IV) and dimethyl ester of 2-methyldiethylsilylethylboric acid (V). To 10.2 g (0.028 mole) of the n-butyl ester of di-(2-methyldiethylsilylethyl)-thioboric acid (b. p. 163-166° at 0.5 mm) was added 5 ml (0.125 mole) of anhydrous methanol, when heat was evolved. Fractional distillation of the reaction mixture yielded:

1) 1.7 g (30%) of the dimethyl ester of 2-methyldiethylsilylethylboric acid.

B. p. 71-72° at 1.5 mm,  $d_4^{21}$  0.8741,  $n_D^{20}$  1.4335. Found %: C 53.28, 53.30; H 11.52, 11.58; B 5.38.  $C_9H_{23}O_2BSi$ . Calculated %: C 53.49; H 11.47; B 5.35.

2) 4.1 g (48%) of the methyl ester of di-(2-methyldiethylsilylethyl)-boric acid.

B. p. 150-151° at 3.5 mm,  $d_4^{21}$  0.8447,  $n_D^{20}$  1.4558. Found %: C 60.12, 60.20; H 12.60, 12.51; B 3.57.  $C_{15}H_{25}OBSi_2$ . Calculated %: C 59.99; H 12.42; B 3.60.

In addition, n-butyl mercaptan and methyltriethylsilane were obtained during the experiment.

7. n-Butyl ester of di-(2-methyldiethylsilylethyl)-boric acid (VI) and di-n-butyl ester of 2-methyldiethylsilylethylboric acid (VII). n-Butanol (11 ml, 0.014 mole) was added dropwise from a dropping funnel to the n-butyl ester of di-(2-methyldiethylsilylethyl)-thioboric acid (9.1 g, 0.025 mole), when heat was evolved. The mixture was then boiled for 2 hr. Fractional distillation of the reaction products yielded:

1) 2.6 g of n-butyl mercaptan with b. p. 95-104°.

2) 2.1 g of methyltriethylsilane with b. p. 120-126°.

3) The n-butyl ester of di-(2-methyldiethylsilylethyl)-boric acid.

B. p. 163-166° at 3.5 mm,  $d_4^{20}$  0.8525,  $n_D^{20}$  1.4538. Found %: C 62.72, 62.98; H 12.45, 12.71; B 3.66, 3.50.  $C_{18}H_{25}OBSi_2$ . Calculated %: C 63.16; H 12.66; B 3.16.

4) The di-n-butyl ester of 2-methyldiethylsilylethylboric acid.

B. p. 150-154° at 5.5 mm,  $n_D^{20}$  1.4375. Found %: C 62.68, 68.72; H 12.11, 12.22; B 4.23, 4.25.  $C_{15}H_{25}O_2BSi$ . Calculated %: C 62.93; H 12.33; B 3.78.

As the esters obtained have very similar boiling points, they could only be separated by repeated fractional distillation, and therefore their yields were not determined.

8. Tri-(2-methyldiethoxysilylethyl)-boron (X). Over a period of 5 hr, 15.3 g (0.094 mole) of vinylmethyldiethoxysilane was added dropwise to 6 g (0.033 mole) of triisobutylboron at 140-145°. The reaction products were then fractionated. The yield was 3.4 g (21.4%).

B. p. 115-118° at 0.01 mm,  $d_4^{20}$  0.9409,  $n_D^{20}$  1.4270. Found %: C 49.90, 49.70; H 10.36, 10.34.  $C_{21}H_{51}O_6BSi_3$ . Calculated %: C 51.01; H 10.34.

We obtained 4 g (77%) of butylene during the experiment.

9. Tri-(2-methyldichlorosilylethyl)-boron (XI). Over a period of 5 hr, 20 g (0.014 mole) of vinylmethyldichlorosilane was added dropwise to 8.6 g (0.047 mole) of triisobutylboron at 140-145°. Fractional distillation yielded 5.1 g (25%) of product with b. p. 127-130° at 0.05 mm (decomp.).

Found %: C 22.91, 22.62; H 4.81, 4.85.  $C_9H_{21}Cl_4BSi_3$ . Calculated %: C 24.71; H 4.80.

We obtained 6 g of butylene during the experiment.

#### SUMMARY

1. Heating vinylmethyldiethylsilane with triisobutylboron yielded tri-(2-methyldiethylsilylethyl)-boron.
2. Tri-(2-methyldiethylsilylethyl)-boron reacted with n-butyl mercaptan to form the n-butyl ester of di-(2-methyldiethylsilylethyl)-thioboric acid.
3. The n-butyl ester of di-(2-methyldiethylsilylethyl)-thioboric acid was converted to di-(2-methyldiethylsilylethyl)-boric acid by the action of water.
4. The n-butyl ester of di-(2-methyldiethylsilylethyl)thioboric acid formed a mixture of esters of di-(2-methyldiethylsilylethyl)-boric and 2-methyldiethylsilylethylboric acids when treated with alcohols.
5. Heating triisobutylboron with vinylmethyldiethoxysilane and vinylmethyldichlorosilane yielded tri-(2-methyldiethoxysilylethyl)-boron and tri-(2-methyldichlorosilylethyl)-boron, respectively.

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## LXIII. REACTIONS OF ALKYLTHIOBORIC ESTERS WITH AMINES

Original article submitted January 3, 1960

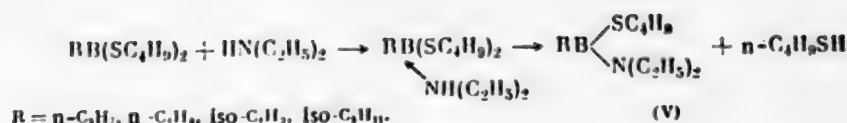
$$RB(SC_4H_9)_2 + 2H_2NR' \rightarrow RB(NHR')_2 + 2n-C_4H_9SH.$$

(1)

$R = n-C_4H_9, n-C_6H_{13}, iso-C_6H_{13}; R' = C_6H_5, n-C_6H_{13}.$

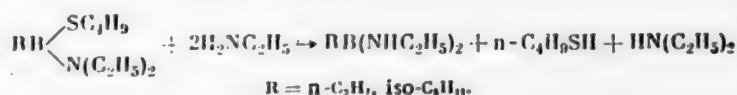
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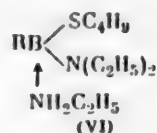


This reaction proceeded smoothly when equimolecular amounts of the reagents were mixed in the cold. The second alkylthio group could not be replaced even by prolonged boiling of a mixture of alkylthioboric ester with excess diethylamine.

Alkyldiethylaminothioboric esters (V), which were stable toward diethylamine, were able to react with ethylamine, and when excess amine was used both the alkylthio and the diethylamino groups were replaced by an ethylamino group to form N-ethyl derivatives of an alkylborodiamine.

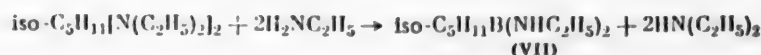


The different behavior of alkyldiethylaminothioboric esters (V) toward ethylamine and diethylamine is apparently connected with the fact that ethylamine is capable of reacting with the esters (V) to form the complex compounds (VI), while diethylamine does not have this property.

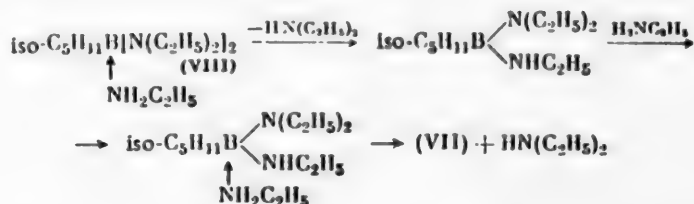


Brown [2] showed that ethylamine shows a greater complex-forming capacity than diethylamine toward organoboron compounds. Thus, for example, ethylamine gives a molecular compound with tri-tert-butylboron, while diethylamine forms no such compound.

The transamination reaction we observed during the reaction of ethylamine and alkyldiethylaminothioboric esters (V) also occurred during the action of ethylamine on isoamyl-di(diethylamino)boron so that isoamyl-di(ethylamino)boron (VII) was formed.

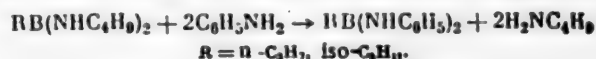


This reaction evidently occurs because the intermediate complex compound (VIII) undergoes the series of irreversible conversions shown in the scheme below.



We then found that the action of aniline on N-alkyl alkylborodiamines yielded N-phenyl alkylborodiamines.

This reaction was carried out by heating the components and distilling the aliphatic amines formed from the reaction mixture. In this way, n-propyl-di(phenylamino)boron and isoamyl-di(phenylamino)boron were synthesized from n-propyl-di(butylamino)boron and isoamyl-di(butylamino)boron, respectively, and aniline.



## EXPERIMENTAL

All operations with organoboron compounds were carried out in a nitrogen atmosphere.

**1. Isobutylboron dibromide.** Isobutylboron dibromide was synthesized by the method we described previously [3]. From 23.4 g of isobutylboric anhydride and 45 g of boron tribromide in n-hexane we obtained 26.4 g (41.6%) of isobutylboron dibromide.

B. p. 54-54.5° (44 mm),  $n_D^{20}$  1.4670,  $d_4^{20}$  1.572. Found %: C 19.86; H 4.00; B 4.49; Br 70.01.  $C_4H_9BBr_2$ . Calculated %: C 21.10; H 3.98; B 4.75; Br 70.17.

**2. Di-n-butyl isobutylthioborate.** We synthesized this compound by the method described previously [1]. From 15.7 g of isobutylboron dibromide and 15.8 g n-butyl mercaptan we obtained 12.3 g (72.8%) of di-n-butyl isobutylthioborate.

B. p. 108-110° (1 mm),  $n_D^{20}$  1.4919,  $d_4^{20}$  0.9020. Literature data [4]: b. p. 142° (3.5 mm),  $n_D^{20}$  1.4919,  $d_4^{20}$  0.9020.

**3. n-Propyldi(n-butylamino)boron.** a) A mixture of 15.6 g of di-n-butyl n-propylthioborate and 13.3 g of n-butylamine was boiled for 3 hr. After removal of the n-butyl mercaptan and excess amine, the residue was distilled twice. We obtained 10.7 g (75.7%) of n-propyldi(n-butylamino)boron.

B. p. 110-111° (11 mm),  $n_D^{20}$  1.4381,  $d_4^{20}$  0.8041. Found %: C 66.43, 66.20; H 13.65, 13.74; B 5.07, 5.05.  $C_{11}H_{27}BN_2$ . Calculated %: C 66.62; H 13.74; B 5.46.

b) n-Propyldi(n-butylamino)boron was also obtained by the action of n-butylamine on n-propylboron dichloride. Under the conditions described previously [5], from 19.7 g of n-propylboron dichloride and 55.4 g of n-butylamine in n-hexane we obtained 3.2 g (10%) of n-propyldi(n-butylamino)boron with b. p. 96.5-98° (6 mm),  $n_D^{20}$  1.4381.

**4. n-Butyldi(ethylamino)boron.** To a mixture of 10.6 g of dibutyl n-butylthioborate and 10 ml of isopentane, cooled to -30°, was added 20 ml of ethylamine. A precipitate was formed, and this disappeared when the reaction mixture was kept at 0°. On the following day, the solvent, excess amine, and n-butyl mercaptan were distilled from the reaction mixture and the residue was vacuum distilled. We obtained 5.4 g of n-butyldi(ethylamino)boron (80.3%) with b. p. 74° (14 mm),  $n_D^{20}$  1.4308,  $d_4^{20}$  0.7990.

The substance was obtained previously by the action of ethylamine on n-butyl n-butylchloroborate [6].

**5. Isoamyldi(n-butylamino)boron.** To 12.7 g of di-n-butyl isoamylthioborate [1] was slowly added 7.4 g of n-butylamine, and heat was evolved. The n-butyl mercaptan (8.6 g) was distilled from the reaction mixture. Fractional distillation of the residue yielded 6.1 g (55.5%) of isoamyldi(n-butylamino)boron.

B. p. 93.5-94° (2 mm),  $n_D^{20}$  1.4422,  $d_4^{20}$  0.8078. Found %: C 69.28, 69.27; H 14.03, 14.11; B 4.82, 4.99.  $C_{13}H_{31}BN_2$ . Calculated %: C 69.02; H 13.81; B 4.78.

**6. n-Butyl n-propyldiethylaminothioborate.** To a mixture of 9.4 g of di-n-butyl n-propylthioborate [1] and 6 ml of isopentane, cooled with ice water, was added 3 g of diethylamine diluted with 10 ml of isopentane. After the reaction mixture had been stirred at room temperature for 1 hr, the solvent and n-butyl mercaptan were distilled from it and the residue was distilled. We obtained 7.4 g (85%) of n-butyl n-propyldiethylaminothioborate.

B. p. 96-97.5° (4 mm),  $n_D^{20}$  1.4704,  $d_4^{20}$  0.8628. Found %: C 61.35, 61.06; H 12.35, 12.07; S 14.36; N 6.79, 6.79.  $C_{11}H_{25}BSN$ . Calculated %: C 61.43; H 12.18; S 14.86; N 6.51.

When a mixture of di-n-butyl n-propylthioborate and diethylamine (0.07 mole) was boiled for 7 hr, we obtained an 85% yield of n-butyl n-propyldiethylaminothioborate with b. p. 96-97.5° (4 mm),  $n_D^{20}$  1.4704,  $d_4^{20}$  0.8628.

**7. n-Butyl n-butyldiethylaminothioborate.** After a mixture of 14 g of di-n-butyl n-butylthioborate [1] and 5.7 g of diethylamine had been stirred at room temperature for 1 hr, then n-butyl mercaptan (99% yield) was distilled from the reaction mixture. The residue was vacuum distilled. We obtained 11.1 g (85.5%) of n-butyl n-butyldiethylaminothioborate.

b. p. 102-103° (3 mm),  $n_D^{20}$  1.4702,  $d_4^{20}$  0.8620. Found %: C 63.17, 62.83; H 12.40, 12.38; N 6.33, 6.62.  $C_{12}H_{23}BNS$ . Calculated %: C 62.88; H 12.32; N 6.16.

Boiling a mixture of 7.8 g of diethylamine and 10 g of di-n-butyl n-butylthioborate for 10 hr and distilling the reaction products yielded 7.65 g (81.3%) of n-butyl n-butylthioborate.

b. p. 116-117° (5 mm),  $n_D^{20}$  1.4702,  $d_4^{20}$  0.8620.

8. n-Butyl isobutylthioborate. A mixture of 8.7 g of di-n-butyl isobutylthioborate and 2.7 g of diethylamine was stirred at room temperature for 1 hr. Distillation of the reaction products yielded 3.13 g (97%) of n-butyl mercaptan and 7.8 g (96.5%) of n-butyl isobutylthioborate.

b. p. 104-106.5° (4 mm),  $n_D^{20}$  1.4700,  $d_4^{20}$  0.8613. Found %: C 62.81; H 12.22; N 6.18.  $C_{12}H_{23}BNS$ . Calculated %: C 62.88; H 12.32; N 6.16.

9. n-Butyl isoamylthioborate. A mixture of 26 g of di-n-butyl isoamylthioborate and 7.3 g of diethylamine was stirred at room temperature for 1 hr. The n-butyl mercaptan was distilled from the reaction mixture under slightly reduced pressure. Distillation of the residue yielded 19.8 g (81.5%) of n-butyl isoamylthioborate.

b. p. 97-98° (2 mm),  $n_D^{20}$  1.4688,  $d_4^{20}$  0.8572. Found %: C 64.27, 64.02; H 12.51, 12.55; N 5.96, 6.20.  $C_{13}H_{25}BNS$ . Calculated %: C 64.18; H 12.43; N 5.76.

After a mixture of 10.7 g of di-n-butyl isoamylthioborate and 5.7 g of diethylamine had been boiled for 30 min, from the reaction products we isolated 8.8 g (88%) of n-butyl isoamylthioborate with b. p. 129-132° (9 mm). After redistillation, the substance had b. p. 104.5° (3 mm),  $n_D^{20}$  1.4688.

10. n-Propylthioborate. To a stirred mixture of 13.7 g of n-butyl n-propylthioborate and 15 ml of isopentane, cooled to -30°, was added 8.5 g of ethylamine. The reaction mixture was stirred at 0° for 1 hr and left overnight. Fractional distillation of the reaction mixture yielded 5.91 g (65.9%) of n-propylthioborate.

b. p. 66-67° (12 mm),  $n_D^{20}$  1.4272,  $d_4^{20}$  0.7908. Found %: C 59.33; H 13.31; B 7.68; N 19.68.  $C_7H_{13}BN_2$ . Calculated %: C 59.16; H 13.49; B 7.62; N 19.72.

11. Isoamylthioborate. A solution of 3.5 g of ethylamine in 5 ml of isopentane was added with stirring to 6.6 g of n-butyl isoamylthioborate in 6 ml of isopentane at -30°. The reaction mixture was stirred at 0° for 1 hr and then boiled for half an hour. Distillation yielded a fraction which had an amine odor and boiled at 60-64° (4 mm). It weighed 2.8 g (61%). After redistillation, the isoamylthioborate had b. p. 53-54° (3 mm),  $n_D^{20}$  1.4332 [5].

12. Preparation of isoamylthioborate from isoamylthioborate. To 4.5 g of isoamylthioborate at -25° was added 5 ml of ethylamine. The reaction mixture was stirred for half an hour and left overnight. It was then boiled for 1 hr and distilled to yield 1.8 g of isoamylthioborate with b. p. 82-84° (15 mm),  $n_D^{20}$  1.4332 [5].

13. Preparation of isoamylthioborate from isoamylthioborate. A mixture of 8.5 g of isoamylthioborate and 7.5 g of aniline was heated in a flask with a fractionating column and distillation condenser. From the reaction mixture we distilled 4.8 g (88.7%) of n-butylamine with  $n_D^{20}$  1.401. Distillation of the residue yielded 8.5 g of isoamylthioborate with b. p. 164-174° (2 mm). After redistillation, the substance had b. p. 173-173.5° (2 mm),  $n_D^{20}$  1.5700. According to literature data [5]:  $n_D^{20}$  1.5700.

14. Preparation of n-propylthioborate from n-propylthioborate. Under analogous conditions, from 9.25 g of n-propylthioborate and 8.8 g of aniline we obtained n-butylamine (79.4%) and n-propylthioborate with b. p. 133-134° (0.35 mm),  $n_D^{20}$  1.5820, which was obtained previously by the action of aniline on n-butyl n-propylchloroborate [6].

## SUMMARY

1. Alkylthioboric esters react with primary aliphatic amines to form N-alkyl alkylborodiamines.



2. The action of diethylamine on alkylthioboric esters forms alkyl-diethylaminothioboric esters, which are a new type of organoboron compound.
3. Alkyl-diethylaminothioboric esters react with ethylamine to form N-ethyl derivatives of alkylborodiamines.
4. The action of ethylamine on an alkyl-di(diethylamino)boron produces transamination which forms an alkyl-di(ethylamino)boron.
5. When heated with aniline, an alkyl-di(n-butylamino)boron undergoes transamination with the formation of N-phenyl derivatives of an alkylborodiamine.

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## ORGANOBORON COMPOUNDS

### LXIV. REACTION OF UNSATURATED ORGANOBORIC ESTERS WITH SILANES

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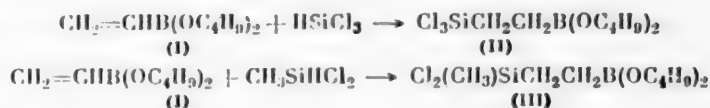
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 11, pp. 3624-3628,

November, 1960

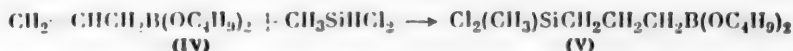
Original article submitted January 3, 1960

Silanes are known to add to unsaturated compounds in the presence of chloroplatinic acid [1-3] and other platinum catalysts. We used this reaction to prepare organosilicoboron compounds.

The reaction of isobutyl vinylborate (I) with trichlorosilane and methyldichlorosilane in the presence of chloroplatinic acid yielded the isobutyl esters of 2-trichlorosilylethylboric (II) and 2-methyldichlorosilylethylboric (III) acids, respectively.



Methyldichlorosilane reacted analogously with n-butyl allylborate (IV) to form n-butyl 3-methyldichlorosilylpropylborate (V).

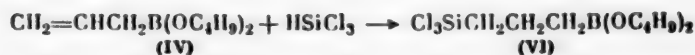


The substances obtained were assigned the given structure in analogy with data on the order of addition of halosilanes to olefins [1-3]; in these cases the trichlorosilyl and methyldichlorosilyl groups add to the terminal carbon atoms.

Trichlorosilane and methyldichlorosilane added to unsaturated organoboric esters under much milder conditions than to olefins, and this is evidently explained by the activating effect of the boron atom on the double bond. However, no addition occurred under the same conditions but in the absence of catalysts. Triethylsilane added to the allylboric ester with much more difficulty in the presence of chloroplatinic acid. When an equimolecular mixture of  $(\text{C}_2\text{H}_5)_3\text{SiH}$  and (IV) had been heated at 80-85° for 4 hr in the presence of the catalyst, only an insignificant amount of organosilicoboron compound was isolated.

It should be noted that the addition of trichlorosilane and methyldichlorosilane to the esters (I) and (IV) was complicated by side processes, which made it difficult to isolate the reaction products in a pure form.

The reaction of trichlorosilane with butyl allylborate was most complex; in this case we obtained a mixture of products from which we isolated a fraction containing more chlorine than the expected n-butyl 3-trichlorosilylpropylborate (VI).

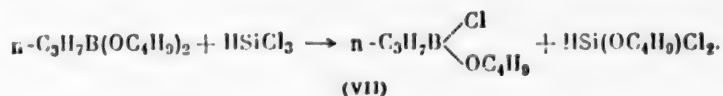


When the reaction was carried out under milder conditions (heating at 35-40° with a tenth of the catalyst), the bulk of the starting materials was recovered.

In view of data [4] on the smooth addition of trichlorosilane and methyldichlorosilane to olefins under the action of  $\gamma$ -radiation, an attempt was made to effect the addition of trichlorosilane to (I) and (IV) under the action of  $\gamma$ -rays. Complex mixtures of substances were obtained in both cases. By repeated distillation, from the reaction products of butyl allylborate and trichlorosilane we isolated a fraction which boiled over a range of 2.5°, but contained more chlorine than the ester (VI).

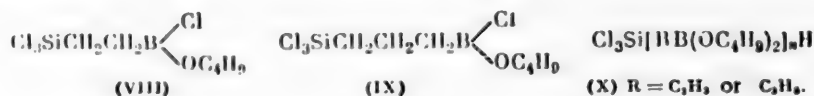
The formation of substances with a high chlorine content by the reaction of the allylboric ester and trichlorosilane both in the presence of catalyst and under the action of  $\gamma$ -radiation compelled us to assume that not only the double bonds, but also the ester groupings participated in the reactions of unsaturated organoboric esters.

To check this hypothesis we studied the reaction of trichlorosilane with *n*-butyl-*n*-propylborate. The experiments were carried out under more drastic conditions than those used in the reactions of unsaturated organoboric esters. When butyl propylborate was boiled with two equivalents of trichlorosilane for 16.5 hr, about 40% of the ester remained unchanged. The remainder of the ester was converted to a chlorine-containing organoboron compound, from which we isolated *n*-butyl *n*-propylchloroborate (VII) in 26% yield, and this was evidently formed by the reaction:



In addition, we obtained a high-boiling substance with a molecular weight of 493, which contained boron, silicon, and chlorine. The structure of the latter was not established. As was to be expected, chloroplatinic acid had no appreciable effect on the reaction studied.

The capacity of an organoboric ester to exchange an alkoxy group for a chlorine atom under the action of trichlorosilane with the formation of a chloro ester (VII) makes it possible to understand the complex course of the reaction between unsaturated organoboric esters and trichlorosilane. It is probable that together with the addition products (II, VI) of trichlorosilane and the esters, there are also formed the butyl esters of trichlorosilyl ethylchloroboric (VIII) or trichlorosilyl propylchloroboric (IX) acids. In addition, the chloroesters arising during the reaction, which have a higher reactivity, may undergo further reaction both with the starting materials and the addition products of the trichlorosilane and the ester. There is also the possibility of telomerization products of the type (X).



#### EXPERIMENTAL

The experiments were carried out in a nitrogen atmosphere. The catalyst used was a 0.1 M solution of  $\text{H}_2\text{PtCl}_6 \cdot 6\text{H}_2\text{O}$  in anhydrous isopropanol. The allyl- and vinylboric esters were synthesized by methods described previously [5, 6].

1. Isobutyl 2-trichlorosilyl ethylborate (II). Over a period of 30 min, 16.6 g of trichlorosilane was added to a stirred mixture of 15 g of isobutyl vinylborate and 0.05 ml of catalyst; the temperature of the mixture rose spontaneously from 20 to 26°. The liquid was stirred for 2.5 hr at room temperature and then boiled on a water bath for 30 min (80-85°). After removal of the unreacted trichlorosilane, the mixture was vacuum distilled from a Favorskii flask. The following fractions were obtained: 1st, 55-118° (4 mm), 1.4 g; 2nd, 118-125° (4 mm), 19 g; 3rd, 125-136° (4 mm), 2.3 g. The residue (2.4 g) solidified in the distillation flask. The second fraction was isobutyl 2-trichlorosilyl ethylborate. The yield was 72.5%. Redistillation yielded 12.1 g (46.2%) of ester.

B. p. 115-118° (3 mm),  $n_D^{20}$  1.4385,  $d_4^{20}$  1.0775. Found %: C 37.86, 38.10; H 7.13, 7.30; Cl 32.41, 32.52, M 312, 313.  $\text{C}_{10}\text{H}_{22}\text{O}_2\text{BCl}_3\text{Si}$ . Calculated %: C 37.58; H 6.93; Cl 33.29, M 319.5.

In another experiment the reaction mixture was heated on a boiling water bath for 3 hr. Distillation yielded the following fractions: 1st, 43-120° (4 mm), 3 g; 2nd, 120-141° (4 mm), 12.6 g; 3rd, 141-155° (4 mm), 5.3 g. Further fractional distillation yielded 6.2 g (23.7%) of isobutyl 2-trichlorosilylethylborate with b. p. 116-120° (3 mm).

The ester was a colorless, mobile liquid, which fumed in air and dissolved readily in diethyl ether and hydrocarbons. The addition of water to an ether solution of isobutyl 2-trichlorosilylethylborate produced a voluminous white precipitate, which dissolved with further addition of water.

2. Isobutyl 2-methyldichlorosilylethylborate (III). Over a period of 15 min, 9.4 g of methyldichlorosilane was added to a stirred mixture of 9.8 g of isobutyl vinylborate and 0.05 ml of catalyst; the temperature was kept at 18-22° by cooling the mixture with water. The liquid was stirred for 30 min without cooling, then heated slowly to boiling over a period of 2 hr, and boiled at 82-85° for 30 min. The excess methyldichlorosilane was distilled from the mixture and the residue vacuum distilled. We isolated two fractions: 1st 55-127° (3 mm), 3.1 g; 2nd, 127-133° (3 mm), 8.9 g. The second fraction was isobutyl 2-methyldichlorosilylethylborate. The yield was 56%. Redistillation yielded 5 g (31.5%) of a colorless liquid which fumed in air.

B. p. 128-130° (3 mm),  $n_D^{20}$  1.4370,  $d_4^{20}$  0.9915. Found %: C 44.85, 44.61; H 8.67, 8.57; Cl 22.24, 22.15.  $C_{11}H_{25}O_2BCl_2Si$ . Calculated %: C 44.16; H 8.42; Cl 23.71.

3. n-Butyl 3-methyldichlorosilylpropylborate (V). A 20.1 g sample of butyl allylborate was mixed at -15° with 0.03 ml of catalyst and 17.7 g of methyldichlorosilane; the mixture was stirred for 30 min at -15°, 1 hr at 2-5°, and then heated to 80° for 30 min. After removal of the methyldichlorosilane, the liquid was vacuum distilled. We obtained the following fractions: 1st, 50-136° (22 mm), 2.1 g; 2nd, 50-70° (0.02 mm), 0.8 g; 3rd, 70-77° (0.02 mm) 20.3 g; 4th, 77-95° (0.02 mm), 7 g.

The third fraction was n-butyl 3-methyldichlorosilylpropylborate. The yield was 64%. After redistillation, the substance had the following constants:

B. p. 77-80° (0.06 mm),  $n_D^{20}$  1.4400,  $d_4^{20}$  0.9684. Found %: C 46.70, 47.19; H 8.87, 8.99; Cl 21.67, 21.88.  $C_{12}H_{27}O_2BCl_2Si$ . Calculated %: C 46.03; H 8.69; Cl 22.64.

4. Reaction of n-butyl allylborate with trichlorosilane. a) Under the action of radiation. A mixture of 19.8 g of n-butyl allylborate and 40.5 g of trichlorosilane in a sealed ampoule was irradiated with  $Co^{60}$   $\gamma$ -rays. The integral dose was  $35 \cdot 10^6$  roentgens. Three distillations yielded 3 g of a fraction with b. p. 67.5-70° (0.06 mm), which was probably butyl 3-trichlorosilylpropylchloroborate (IX) with some 3-trichlorosilylboric ester (VI).

Found %: C 31.45, 31.16; H 5.81, 5.68; Cl 41.84, 42.16.  $C_7H_{15}OBCl_3Si$ . Calculated %: C 28.41; H 5.11; Cl 47.93.  $C_{11}H_{24}O_2BCl_3Si$ . Calculated %: C 39.60; H 7.25; Cl 31.89.

b) In the presence of catalyst. Over a period of 45 min, 17.5 g of n-butyl allylborate was added to a stirred mixture of 17.5 g of trichlorosilane and 0.05 ml of catalyst. During the addition, the temperature of the mixture rose from 18 to 23°. The mixture was stirred at room temperature for 1.5 hr and then heated to 75° for 1 hr. Distillation yielded the following fractions: 1st, 42-102° (7 mm), 1.8 g; 2nd 97-126° (3 mm), 1.6 g; 3rd, 126-140° (3 mm), 3.4 g; 4th, 140-167° (3 mm), 9.7 g; 5th, 167-181° (3 mm), 5.2 g.

The third fraction, which contained 38.3% of chlorine, was probably a mixture of the n-butyl esters of 3-trichlorosilylpropylchloroboric and 3-trichlorosilylpropylboric acids as in the previous case. The fourth fraction contained 27.8% of chlorine and the 5th fraction, 24% of chlorine.

5. Reaction of n-butyl n-propylborate and trichlorosilane. Into a flask with a reflux condenser and a nitrogen inlet were placed 24 g of n-butyl propylborate and 32.4 g of trichlorosilane and the mixture boiled for 16.5 hr; the boiling point of the mixture gradually rose from 49 to 66°. After the heating, the trichlorosilane was distilled from the mixture (18.7 g, b. p. 34-38°), and the residue was vacuum distilled twice to yield the following fractions: 1st, 62-66° (24 mm), 5.32 g,  $n_D^{20}$  1.4122; 2nd, 66-102° (24 mm), 5.5 g; 3rd, 102-108° (24 mm), 9.9 g,  $n_D^{20}$  1.4115; 4th, 86-136° (3 mm), 4.6 g,  $n_D^{20}$  1.4170; 5th, 136-160° (3 mm), 4.2 g,  $n_D^{20}$  1.4263, 6th, 160-166° (3 mm), 1.9 g,  $n_D^{20}$  1.4392.

The first fraction was n-butyl n-propylchloroborate (according to literature data [7]: b. p. 60.5-61° at 22 mm and  $n_D^{20}$  1.4120°); the third fraction was the starting n-butyl n-propylborate (according to literature data [7]: b. p. 82-83° at 7 mm and  $n_D^{20}$  1.4110°); the sixth fraction contained boron, silicon, and chlorine. \* The refractive index of the substance synthesized by B. M. Mikhailov and T. A. Shchegoleva [7] is given.

## SUMMARY

1. Butyl esters of vinyl- and allylboric acids add methylchlorosilane and trichlorosilane in the presence of chloroplatinic acid to form organoborosilicon compounds. By this method we synthesized the butyl esters of 2-methylchlorosilylethylboric, 2-trichlorosilylethylboric, and 3-methylchlorosilylpropylboric acids.

2. Silanes add to unsaturated organoboric esters under milder conditions than to olefins.

3. Butyl n-propylborate reacts with trichlorosilane with heating to form butyl n-propylchloroborate and other, unidentified products.

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## SYNTHESES OF ISOXANTHINE DERIVATIVES

### V. ISOCAFFEINE-8-MALONIC ESTER AND AMIDES OF ISOCAFFEINE-8-ACETIC ACID

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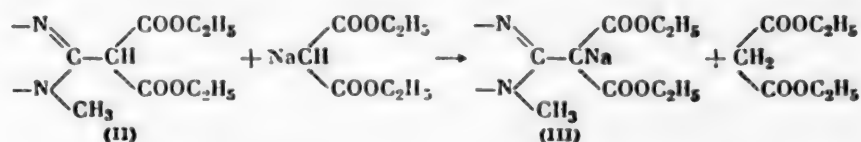
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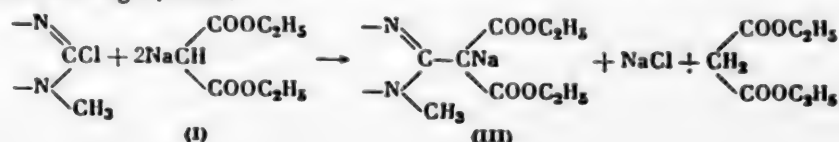
Original article submitted January 5, 1960

In order to synthesize some derivatives of methylated isoxanthine substituted at C<sub>8</sub> through a carbon-carbon bond with various residues, including alkanolic acids and derivatives of alkanolic acids and derivatives of alkanolic acids, we undertook the condensation of 8-chloroisocaffeine (I) with sodiummalonic ester. It was found that as in the analogous condensation of the isomeric 8-chlorocaffeine with the double bond between positions 8 and 9 [1], the reaction showed certain peculiarities which were associated with the comparatively high acidity of the isocaffeine-8-malonic ester (II) obtained. This ester dissolved readily in dilute alkali solutions and was recovered unchanged on acidification, while its sodium derivative (III) was quite a stable compound which could be recrystallized from water successfully.

The reason for the quite high degree of dissociation of the unsubstituted hydrogen in the malonic part of the molecule of (II), which distinguishes this compound from other monosubstituted derivatives of malonic ester (for example, monoalkylmalonic esters), is apparently the effect of the electron-acceptor groups (in particular, C=O) of the purine part of the molecule (II) on the malonic residue, which is transmitted through the system of conjugated double bonds and causes a redistribution of the electron density in this residue, with a corresponding increase in the polarity of the C-H bond. This effect is the reason why the isoxanthine ring as a whole acts as an electronegative group toward its substituents at C<sub>8</sub>. In the given case, the direct result of this effect of the ring was that during the condensation, substance (II) separated from the reaction mixture as its sodium derivative (III); the source of sodium for the conversion of (II) to (III) was sodiummalonic ester, as malonic ester is a much weaker acid than substance (II).

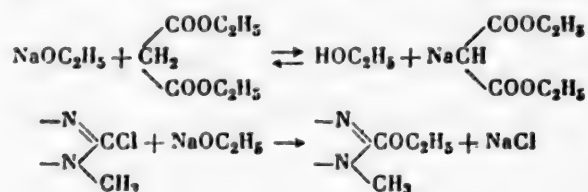


From the equation presented it follows that the preparation of (II) requires 2 moles of sodiummalonic ester to 1 mole of 8-chloroisocaffeine (I) for completion, as only half of the sodiummalonic ester used can participate in the condensation, while the second half is consumed in the conversion of the condensation product to its sodium derivative. Otherwise, i.e., with equimolecular amounts of the reagents, not less than 50% of the starting (I) is recovered from the reaction. The successive reactions which occur during the condensation may be summarized by the following equation.

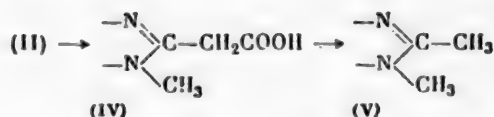




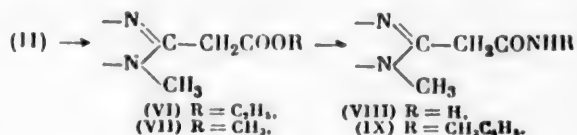
The use of a slight excess (10-15%) of sodiummalonic ester above the calculated 2 moles made it possible to obtain substance (II) in about 80% yield. It was advantageous to carry out the reaction in dry toluene, from which the isocaffeine-8-sodiummalonic ester (III) separated quantitatively even during heating, as it is completely insoluble in most organic solvents. This condensation could not be carried out in anhydrous alcohol because substance (I) reacts more rapidly with sodium ethylate than with sodiummalonic ester due to the fact that the equilibrium of the system sodium ethylate  $\rightleftharpoons$  sodiummalonic ester is displaced to the left and practically the whole of substance (I) used for the reaction is converted into 8-ethoxyisocaffeine [2].



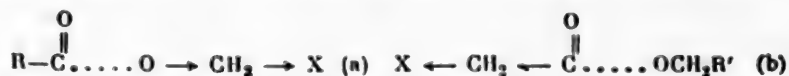
For hydrolysis and partial decarboxylation, the diester (II) was heated with mineral acids in an aqueous or alcohol medium. When (II) was heated with 18-20% aqueous hydrochloric acid, both carbethoxyl groups were hydrolyzed and 1 mole of  $\text{CO}_2$  was eliminated simultaneously. The isocaffeine-8-acetic acid (IV) formed was comparatively unstable and readily decarboxylated; therefore, it was partly converted into 8-methylisocaffeine (V) during the hydrolysis process.



The results obtained by heating the diester (II) with an alcohol solution of HCl differed in that only one of the ester groupings was eliminated while the second remained unchanged. This method guaranteed the retention of the second carboxyl group and was particularly convenient when the acid (IV) was used for subsequent reactions in the form of the ester (VI). An example of these reactions is the conversion of isocaffeine-8-acetic esters into amides of the acid.



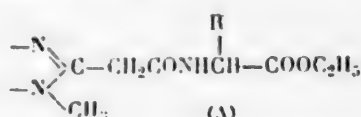
The unsubstituted amide (VIII) was readily formed in high yield even at room temperature by shaking the esters (VII) and (VI) with an aqueous solution of ammonia. The capacity of the esters (VI) and (VII) to react with ammonia under mild conditions confirms to some extent the hypothesis presented above on the capacity of the isocaffeine ring to act as an electron acceptor and cause a redistribution of electron density in substituents attached to it at position 8; it indicates that there is some analogy between the reasons for the activity of these esters and the mechanism of the activation of esters by the accepted mode when the weakening of the bond of the carbonyl C atom with the oxygen of the alkoxy group is caused by the introduction of an electrophilic atom or group of atoms (for example,  $-\text{CN}$  [3]) into the alkoxy part of the ester grouping [scheme (a)]. The essential difference in the given case is apparently the fact that according to scheme (b) the electron cloud should be displaced in the opposite direction, i.e., toward the ring and not toward the alkoxy group.



X is an electronegative substituent.

In addition, the isocaffeine ring produces a comparatively low degree of activation of the esters (VI) and (VII), which, in particular, is insufficient for their amidation by esters of amino acids. In order to prepare the

group of substituted amides (A), it was necessary to resort to such a strong method of activating (IV) as preparing its mixed anhydride with phosphorodichloridic acid [4].



Alkaline hydrolysis of these amides yielded the amino acids glycine, valine, and phenylalanine acylated with isocaffeine-8-acetic acid.

## EXPERIMENTAL

**Isocaffeine-8-malonic ester (II).** To a suspension of 23 g of finely divided sodium in 600-700 ml of dry toluene was gradually added 230 g of malonic ester, the mixture boiled with vigorous stirring until the formation of the sodiomalonic ester was complete (30-40 min) and cooled to 50-60°, and 100 g of carefully dried substance (I) added. The reaction mixture was boiled and stirred for 10 hr, during which time (I) dissolved and a voluminous crystalline precipitate of the Na derivative of (II) and NaCl formed. The precipitate (~193.5 g) was collected from the cooled mixture and 1 g recrystallized from 5 ml of 96% alcohol. Substance (III) was again recrystallized from alcohol for analysis.

Found %: N 15.15,  $\text{C}_{15}\text{H}_{19}\text{O}_6\text{N}_4\text{Na}$ . Calculated %: N 14.93.

The mixture of (III) and NaCl obtained was dissolved in 1500 ml of warm water (50-35°) and the clear, wine-red solution adjusted to pH 3-4 with 20% mineral acid; the soft white or pinkish crystals thus formed were collected, washed with a small amount of cold water, and dried. The weight was 102 g and the m. p. 133-135°, and after recrystallization from 500 ml of alcohol the substance weighed 94 g and had m. p. 137-138°. Extraction of the aqueous filtrate with chloroform and concentration of the alcohol filtrate from recrystallization (300-350 ml of alcohol was distilled) yielded a further small amount of the ester (II), which had m. p. 137-138° and weighed 15 g after recrystallization from alcohol (1:5-7). The total yield of (II) was 109 g (70.59%).

Found %: N 15.93,  $\text{C}_{15}\text{H}_{20}\text{O}_6\text{N}_4$ . Calculated %: N 15.90.

**Isocaffeine-8-acetic acid (IV).** a) From isocaffeine-8-malonic ester (II). A mixture of 20 g of (II) and 200 ml of 18% hydrochloric acid was boiled and stirred for 15-20 min (until the molten upper layer dissolved completely) and the solution cooled and neutralized with dry  $\text{NaHCO}_3$ . The crystalline precipitate which formed at pH 4-5 was collected and dissolved in 5%  $\text{NaHCO}_3$  solution, the turbid solution treated with charcoal and filtered, and the acid (IV) precipitated by acidification with concentrated hydrochloric acid. The precipitate was collected, washed with cold water and alcohol, and dried in air. The yield was 10.2 g (72%). The m. p. of the acid (IV) was 255-257° (decomp.).

Found %: N 21.79; C 47.07; H 4.82,  $\text{C}_{10}\text{H}_{12}\text{O}_4\text{N}_4$ . Calculated %: N 22.22; C 47.61; H 4.76.

The titration of 0.1900 g of the substance in 15.00 ml of 0.1 N NaOH required 7.63 ml of 0.1 N HCl. Calculated: 7.53 ml of 0.1 N HCl.

b) From a mixture of the Na derivative of isocaffeine-8-malonic ester (III) and NaCl. The crystalline precipitate isolated from the condensation of 20 g of (I) with sodiomalonic ester was boiled for 15 min with 200 ml of 20% hydrochloric acid with stirring (with charcoal for the last 5-6 min); the mixture was filtered and the cooled solution neutralized with dry  $\text{NaHCO}_3$  (to a chestnut color with Congo). The precipitate was collected and dissolved in 120 ml of 5%  $\text{NaHCO}_3$  solution and the solution treated with charcoal, filtered, and acidified with conc. HCl (7.5 ml). The precipitate was collected, washed with glacial acetic acid and then alcohol, and dried in air. The m. p. was 254-255° and the yield was 14.8 g [66.9% on the starting (I)].

The titration of 0.1706 g in 10 ml of 0.1 N NaOH required 6.65 ml of 0.1 N HCl. Calculated: 6.77 ml.

c) From isocaffeine-8-acetic esters (VI) and (VII). To a mixture of 2.74 g of the ester (VI) or (VII), 0.5 ml of alcohol, and 5 ml of water was added 5 ml of 2 N NaOH solution dropwise (to pH 8). Acidification of the alkaline solution precipitated 2.3-2.5 g (~95%) of the acid (IV) with m. p. 256-257°; mixtures with the samples obtained by methods (a) and (b) melted at 256-257°.

Methyl isocaffeine-8-acetate (VII). A mixture of 25 g of the acid (IV), 13 ml of conc.  $\text{H}_2\text{SO}_4$ , and 375 ml of  $\text{CH}_3\text{OH}$  was boiled for 4 hr; the residue was treated with ice, neutralized with dry  $\text{NaHCO}_3$ , and the partly crystalline mass extracted with chloroform. Distillation of the chloroform gave 25 g of a residue with m. p. 192-198°; recrystallization from methanol gave 20.7 g (80.5%) of product with m. p. 202-204° (decomp.). For analysis, the product was recrystallized twice from  $\text{CH}_3\text{OH}$ , when it had m. p. 205-206°.

Found %: N 21.05; C 49.54; H 5.09.  $\text{C}_{11}\text{H}_{14}\text{O}_4\text{N}_4$ . Calculated %: N 21.05; C 49.62; H 5.26.

Ethyl isocaffeine-8-acetate (VI). a) A mixture of 2 g of (II) and 20 ml of an 8% solution of  $\text{HCl}$  in alcohol was boiled for 3 hr. The alcohol was removed and the residue treated with 10-15 ml of water and neutralized with dry  $\text{NaHCO}_3$ . The crystalline substance liberated was collected; it had m. p. 210-212° and the yield was 1.35 g (85%). For analysis, the product was recrystallized from alcohol, when it had m. p. 213-214°.

Found %: N 20.19.  $\text{C}_{12}\text{H}_{16}\text{O}_4\text{N}_4$ . Calculated %: N 20.00.

b) A mixture of 1 g of substance (IV) and 20 ml of a 17% alcohol solution of  $\text{HCl}$  was boiled for 3 hr. The alcohol was removed and the residue treated with water and  $\text{NaHCO}_3$  to yield (VI). After recrystallization from alcohol, the substance had m. p. 213-214°. The yield was 0.57 g (51%). The m. p. of a mixture with the (VI) obtained by method (a) was 213-214°.

Amide of isocaffeine-8-acetic acid (VIII). A mixture of 15 g of the ester (VI) or (VII) and 300 ml of 33-35% ammonia solution was shaken at room temperature for 30 hr. The suspended solid was collected and washed with water and alcohol. The weight was 12.73-10 g (90.00-73.00%) and the product had m. p. 264-267°. For analysis, the product was recrystallized from dimethylformamide (1:10), when it had m. p. 271-272°. It crystallized with 1 mole of dimethylformamide.

Found %: N 25.81; C 48.51; H 5.91.  $\text{C}_{13}\text{H}_{20}\text{O}_4\text{N}_6$ . Calculated %: N 25.92; C 48.14; H 5.86.

N-(isocaffeine-8)-acetylphenylalanine. To a mixture of 5.04 g of (IV), 4.6 g of the hydrochloride of the ethyl ester of phenylalanine, and 2.8 ml of triethylamine in 150 ml of dry methylene chloride at -15 to -12° was rapidly added a mixture of 3.66 g of phosphorus oxychloride and 5.6 ml of triethylamine and the mixture stirred for 1 hr at -15° and 1 hr at 20°. The reaction mixture was washed three times with 10-ml portions of water, the aqueous layer separated, and the washed and dried solution evaporated in vacuum. The residue was triturated with alcohol to yield 4.6 g (54%) of the ethyl ester of N-(isocaffeine-8)-acetylphenylalanine with m. p. 209-211° (from alcohol, 1:9).

Found %: N 16.19.  $\text{C}_{21}\text{H}_{25}\text{O}_5\text{N}_5$ . Calculated %: N 16.38.

A 1 N solution of  $\text{NaOH}$  was added dropwise to a mixture of 2.6 g of unrecrystallized ester (m. p. 208-210°) and 25 ml of alcohol at 55-50° (pH ~8). The cooled and filtered solution was acidified and then diluted with 50 ml of water. The N-(isocaffeine-8)-acetylphenylalanine liberated was recrystallized from 75 ml of water and the dihydrate obtained dried at 120-130°. The yield was 1.99 g (80%) and the m. p. was 231-232° (decomp.). The substance lost water of crystallization at 150°.

Found %: N 16.37;  $\text{H}_2\text{O}$  7.40 (by Fischer's method).  $\text{C}_{19}\text{H}_{21}\text{O}_5\text{N}_5 \cdot 2\text{H}_2\text{O}$ . Calculated %: N 16.31;  $\text{H}_2\text{O}$  8.20.

The reactions with the esters of glycine, valine, and  $\beta$ -alanine and benzylamine were carried out analogously.

Ethyl ester of N-(isocaffeine-8)-acetyl glycine. The yield was 77% and the m. p. 161-163° (from alcohol 1:4).

Found %: N 20.66.  $\text{C}_{14}\text{H}_{19}\text{O}_5\text{N}_5$ . Calculated %: N 20.75.

Hydrolysis of the ester with 1 N  $\text{NaOH}$  solution at room temperature yielded N-(isocaffeine-8)-acetyl glycine as the monohydrate in 71% yield; the m. p. was 274-276° (decomp.).

Found %: N 21.66;  $\text{H}_2\text{O}$  5.20 (by Fischer's method).  $\text{C}_{12}\text{H}_{15}\text{O}_5\text{N}_5 \cdot \text{H}_2\text{O}$ . Calculated %: N 21.40;  $\text{H}_2\text{O}$  5.50.

Ethyl ester of N-(isocaffeine-8)-acetylvaline. The yield was 52% and the m. p. 218-220° (from water).

Found %: N 18.51; C 54.13; H 6.58.  $C_{17}H_{25}O_5N_5$ . Calculated %: N 18.45; C 53.81; H 6.64.

Hydrolysis of the ester with 1 N NaOH at 60-65° yielded N-(isocaffeine-8)-acetylvaline. The yield was 38% and the m. p. 248-250° (decomp.).

Found %: N 19.14; C 50.47; H 5.94;  $H_2O$  2.35 (by Fischer's method).  $C_{15}H_{21}O_5N_5 \cdot 0.5H_2O$ . Calculated %: N 19.42; C 50.00; H 6.10;  $H_2O$  2.50.

Ethyl ester of N-(isocaffeine-8)-acetyl- $\beta$ -alanine. The yield was 17% and the m. p. 190-191° (from methanol).

Found %: N 19.77.  $C_{15}H_{21}O_5N_5$ . Calculated %: N 19.92.

Benzylamide of (isocaffeine-8)-acetic acid (IX). The yield was 61% and the m. p. was 248-250° (from alcohol).

Found %: N 20.46.  $C_{17}H_{19}O_3N_5$ . Calculated %: N 20.50.

#### SUMMARY

1. Condensation of 8-chloroisocaffeine with sodiummalonic ester yielded isocaffeine-8-malonic ester, which, due to its comparatively high acidity, formed a quite stable sodium derivative, which crystallized readily from water.

2. Heating isocaffeine-8-malonic ester with an alcohol solution of hydrogen chloride formed the ethyl ester of isocaffeine-8-acetic acid, i.e., only one carbethoxyl group was eliminated. Hydrolysis in aqueous hydrochloric acid led to hydrolysis of both ester groupings.

3. Glycine, valine, and phenylalanine acylated with isocaffeine-8-acetic acid were synthesized. We also prepared the unsubstituted amide of isocaffeine-8-acetic acid and its benzylamide.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. Some or all of this periodical literature may well be available in English translation. A complete list of the cover-to-cover English translations appears at the back of this issue.

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## BIS(β-CHLOROETHYL)-AMINES OF BICYCLIC COMPOUNDS

### I. BIS(β-CHLOROETHYL)-AMINES OF THE INDAN SERIES

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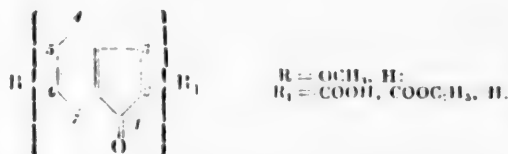
November, 1960

Original article submitted January 1, 1960

Bicyclic systems of condensed nuclei are frequently part of the molecules of natural biologically active substances, and therefore the study of these compounds is of definite interest in the search for new drugs.

The present work was devoted to the synthesis and investigation of 1-aminoindans and some of their derivatives with substituents or without substituents in the aromatic or alicyclic parts of the molecules.

The starting materials were 1-indanones (I), which were converted into oximes and the latter reduced to amines.



The 1-indanones were obtained largely by cyclization of aliphaticaromatic acids. We carried out this reaction with phenylpropionic, phenylsuccinic, and m- and p-methoxy- and 3,4-dimethoxyphenylpropionic acids. Two methods were used for the cyclization: a) cyclization of the free acids with the aid of polyphosphoric acid and b) cyclization of the acid chlorides in the presence of  $\text{AlCl}_3$ .

Substituents in the benzene nucleus are known to have a substantial effect on the course of the reaction in the cyclization of aliphatic-aromatic acids. We encountered similar phenomena in our work. Phenylsuccinic acid could not be cyclized with the aid of polyphosphoric acid despite variations in the reaction conditions. A sufficiently high yield of 3-carboxy-1-indanone could only be obtained when the diacid chloride was used and  $\text{AlCl}_3$  was added as a catalyst. By applying the same methods to phenylpropionic acid according to literature data [1], we obtained 1-indanone in good yield without difficulty. Thus, the substituents in the side chain had an appreciable effect on the capacity of the substance to cyclize.

The cyclization of m-methoxyphenylpropionic acid has been studied by many investigators. L. Nowak and M. Protiwa [2] started from the acid chloride and used  $\text{SnCl}_4$  as the catalyst, while Ingold and Pigott [1] carried out the reaction in the presence of  $\text{AlCl}_3$ . The latter authors considered that there was a possibility of the formation of two isomers: 5-methoxy- and 7-methoxy-1-indanone. These and other investigators obtained 5-methoxy-1-indanone (by cyclization in the position para to the methoxyl group), but the latter investigators were able to isolate dimethylated compounds of 5- and 7-hydroxy-1-indanones from the by-products of the reaction, which indicates slight formation of the second isomer. By carrying out the reaction with free m-methoxyphenylpropionic acid in the presence of polyphosphoric acid, we obtained a good yield of 5-methoxy-1-indanone; the other isomer was not detected.



Isomers could not be formed in the cyclization of *p*-methoxyphenylpropionic acid because of the symmetry of the molecule, but the prospective positions for ring closure were in a position meta to the methoxyl group, which is unfavorable for intramolecular acylation. When we used method "a" we obtained 6-methoxy-1-indanone from *p*-methoxyphenylpropionic acid in not more than 3-8% yield, while when method "b" was used under the conditions described in [3], this ketone was obtained in 60% yield despite the fact that the starting acid chloride was not purified beforehand.

In the cyclization of 3,4-dimethoxyphenylpropionic acid, the two possible positions of ring closure (positions 2 and 6 of the benzene ring relative to the side chain) are affected differently by the two methoxyl groups. On the basis of previous data it can be seen that position 6 is more favorable for cyclization, and therefore it was to be expected that 5,6-dimethoxy-1-indanone would be formed in a predominating amount if not exclusively. In accordance with the directions of J. Koo [1], we carried out the cyclization by method "a" alone, and this indanone was obtained in 95% yield.

In addition to the indanones mentioned above, we prepared 3-carbethoxy-1-indanone by esterification of 3-carboxy-1-indanone.

The oximes of the ketones mentioned were obtained in the usual way. Three methods were used for reduction of the oximes: 1) catalytic reduction with hydrogen in the presence of Raney nickel, 2) reduction with lithium aluminum hydride, and 3) reduction with aluminum amalgam. As the last method was the simplest and gave the best results, most oximes were reduced in this way.

By-products were formed during catalytic reduction. Thus, for example, together with 1-aminoindanone, the reduction of 1-indanone oxime formed a secondary amine, namely 1-di(indanyl)-amine. Similarly, in addition to 3-carboxy-1-aminoindanone, the reduction of 3-carboxy-1-indanone oxime gave another substance, whose structure we did not determine.

In connection with our previous work on alicyclic compounds [4], we were particularly interested in 1-bis( $\beta$ -chloroethyl)-aminoindans. These compounds were prepared by a method which has already been described in detail: the action of ethylene oxide on amines to give dihydroxyethyl derivatives of amines with subsequent replacement of the hydroxyl group by chlorine. However, we were unable to use this method to prepare bis( $\beta$ -chloroethyl) derivatives from 5-methoxy- and 5,6-dimethoxy-1-aminoindans, although the corresponding di-hydroxyethyl compounds were isolated. Instead of 1-bis( $\beta$ -chloroethyl)-aminoindans, in both cases we obtained an aliphatic bis( $\beta$ -chloroethyl)-amine, which indicates the instability of the C-N bond in an acid medium in both of these indan compounds. We observed similar phenomena in other cases in the synthesis of substituted bis( $\beta$ -chloroethyl)-amines. However, the material on this phenomenon is still insufficient for any substantiated theoretical hypotheses, and we limit ourselves to the demonstration of the fact for now.

## EXPERIMENTAL

**3-Carboxyl-1-indanone.** The starting material, phenylsuccinic acid, was obtained by a method described in the literature [5] and its diacid chloride by the method in [6]. To 13.9 g of aluminum chloride suspended in 50 ml of ligroin (b. p. 50-70°) was gradually added 13.9 g of the diacid chloride of phenylsuccinic acid. The reaction mixture was boiled for 2.5 hr. To the cooled mixture was added 50 ml of water and the precipitate collected and recrystallized from water. The m. p. was 117-119°. The yield was 7.4 g (70.5%).

Found %: C 68.27; H 4.56.  $C_{10}H_8O_3$ . Calculated %: C 68.18; H 4.58.

The sodium salt of 3-carboxyl-1-indanone was obtained by dissolving 3-carboxyl-1-indanone in a saturated solution of sodium bicarbonate. After extraction with ether, the aqueous solution was evaporated to dryness. The substance obtained was washed with anhydrous acetone and ether and dried in a vacuum desiccator. The sodium salt was readily soluble in water and hygroscopic. It was insoluble in most organic solvents.

**3-Carboxy-1-indanone oxime.** To a mixture of 1.97 g of hydroxylamine hydrochloride and 2.33 g of sodium acetate in 15 ml of water was gradually added 5 g of 3-carboxy-1-indanone in 25 ml of alcohol and the mixture stirred at room temperature for 3 hr. The colorless precipitate was collected and recrystallized from water. The m. p. was 180° (decomp.). The yield was 4.96 g (91.5%).

Found %: C 62.91; H 4.58; N 7.04.  $C_{10}H_8O_3N$ . Calculated %: C 62.82; H 4.74; N 7.38.



The sodium salt of 3-carboxy-1-indanone oxime was obtained as described above.

Found %: Na 10.65,  $C_{10}H_7O_3NNa$ . Calculated %: Na 10.80.

3-Carbethoxy-1-indanone. A stream of dry hydrogen chloride was passed through a solution of 40 g of 3-carboxy-1-indanone in 200 ml of anhydrous alcohol for 2 hr with heating. Removal of the alcohol left an oil which crystallized on cooling. It had m. p. 44-46° and b. p. 140-145° (3 mm). The yield was 43 g (93%). After two recrystallizations from ligroin the substance melted at 46-48°.

Found %: C 70.40, 70.28; H 5.85,  $C_{12}H_{12}O_3$ . Calculated %: C 70.57; H 5.92.

3-Carbethoxy-1-indanone oxime was obtained by the usual method. The yield was 95.5% and the m. p. was 124-125° (from a mixture of benzene and ligroin).

Found %: C 65.85; H 5.91; N 6.29,  $C_{12}H_{13}O_3N$ . Calculated %: C 65.74; H 5.97; N 6.38.

5-Methoxy-1-indanone. With cooling and stirring, 30 g of phosphorus pentoxide was gradually added to 20 ml of phosphoric acid. The mixture obtained was heated at 100° for 1 hr to yield a clear slumpy mass. The latter was cooled to 70°, 5 g of  $\beta$ -(*m*-methoxyphenyl)propionic acid added, and the mixture kept at this temperature for 30 min. The color of the reaction mixture changed from amber-yellow to dark red. The cooled reaction mixture was gradually added to a cooled 15% aqueous solution of sodium carbonate to a neutral reaction to litmus. The white precipitate was collected, washed with iced water, and dried in a drying cupboard at 70°. It had m. p. 110-112°. The yield was 3.5 g (72.7%). The oxime had m. p. 156-158°.

6-Methoxy-1-indanone was obtained in accordance with [3]. The yield was 67% and the m. p. 108-109° (from alcohol). The oxime had m. p. 133-134.5° [1].

5,6-Dimethoxy-1-indanone was obtained in accordance with [1] from dimethoxyphenylpropionic acid in the presence of polyphosphoric acid. The yield was 95% and the m. p. 118-119° (from water). 5,6-Dimethoxy-1-indanone oxime had m. p. 196-197° (from alcohol). The yield was 93.2%.

Found %: C 63.63; H 6.28; N 6.70,  $C_{11}H_{13}O_3N$ . Calculated %: C 63.75; H 6.27; N 6.76.

1-Aminoindan and di(indanyl-1)amine. A 10-g sample of 1-indanone oxime in 200 ml of anhydrous alcohol was hydrogenated in the presence of 2.5 g of Raney nickel in an autoclave at 70° and an initial hydrogen pressure of 50 atm. The catalyst was removed, the alcohol evaporated and the residual oil vacuum distilled, with measures to protect the amine from atmospheric carbon dioxide. We obtained two fractions: the 1st had b. p. 92-95° (7 mm), 3.2 g (1-aminoindan); the 2nd had b. p. 195-205° (7 mm), 5.5 g [di(indanyl-1)amine]. 1-Aminoindan hydrochloride was obtained by dissolving 1-aminoindan in absolute ether and adding an ether solution of hydrogen chloride. It had m. p. 208°, which agrees with literature data [7]. Di(indanyl-1)amine hydrochloride was obtained analogously. It had m. p. 230° (with charring) (from a mixture of alcohol and ethyl acetate).

Found %: C 74.96; H 7.34; N 4.88; Cl 12.83,  $C_{10}H_{11}N \cdot HCl$ . Calculated %: C 75.58; H 7.08; N 4.90; Cl 12.45.

1-Acetylaminoindan. It had m. p. 123-124° (from aqueous alcohol).

Found %: C 75.21; H 7.44; N 7.92,  $C_{11}H_{13}ON$ . Calculated %: C 75.40; H 7.47; N 7.99.

Acetyl derivative of di(indanyl-1)amine. It had m. p. 206-208° (decomp., from ethyl acetate).

Found %: C 82.87; H 7.45; N 4.83,  $C_{20}H_{22}ON$ . Calculated %: C 82.45; H 7.26; N 4.81.

3-Carboxy-1-aminoindan. A 9-g sample of 3-carboxy-1-indanone oxime in 200 ml of anhydrous alcohol saturated with ammonia was hydrogenated in the presence of 6 g of Raney nickel at 85-90° and a pressure of 150 atm for 3.5 hr. We obtained 5.42 g of 3-carboxy-1-aminoindan with m. p. 270-272° (from alcohol).

Found %: C 68.31; H 6.19; N 7.71,  $C_{10}H_{11}O_2N$ . Calculated %: C 67.96; H 6.21; N 7.90.

After separation of the 3-carboxy-1-aminoindan, from the alcohol mother solution we obtained 4.71 g of a substance with m. p. 170-180°. The substance was not investigated.

3-Carbethoxy-1-aminoindan. To a mixture of 24 g of 3-carbethoxy-1-indanone oxime, 37 g of aluminum amalgam, and 300 ml of absolute ether was added 25 ml of water over a period of 8 hr at the boiling point of

the ether. The reaction mixture was filtered and the amine isolated from the filtrate. It had b. p. 119-120° (2 mm); 130-140° (4 mm). The yield was 18.1 g (82%). The amine hydrochloride had m. p. 190-191° (from alcohol).

Found %: C 59.45; H 6.32; N 5.98; Cl 14.70.  $C_{12}H_{15}O_2N \cdot HCl$ . Calculated %: C 59.62; H 6.70; N 5.79; Cl 14.66.

5-Methoxy-1-aminoindan.\* Analogously, from 16.82 g of 5-methoxy-1-indanone oxime and 50 g of aluminum amalgam we obtained an amine with b. p. 115-118° (2 mm). The yield was 12.5 g (80.7%). The hydrochloride had m. p. 229-230°.

6-Methoxy-1-aminoindan.\* To 6 g of  $LiAlH_4$  in 70 ml of absolute ether was added 10 g of 6-methoxy-1-indanone oxime in 300 ml of absolute ether at such a rate that the ether boiled gently. After the addition, the reaction mixture was kept at the boiling point of the ether for a further 3 hr. The complex formed was carefully decomposed with 60 ml of a 10% solution of sodium hydroxide and the  $Al(OH)_3$  removed by filtration. From the ether we isolated 5.7 g of amine (60.1% yield) with b. p. 110-114° (1.5 mm). 6-Methoxyaminoindan hydrochloride had m. p. 240-242° (decomp.).

Found %: C 60.09; H 7.11; N 7.05; Cl 17.77.  $C_{10}H_{13}ON \cdot HCl$ . Calculated %: C 60.14; H 7.06; N 7.01; Cl 17.75.

5,6-Dimethoxy-1-aminoindan. As described above, from 14 g of 5,6-dimethoxy-1-indanone oxime and 40 g of aluminum amalgam we obtained 11.8 g (90.7%) of an amine with b. p. 132-134° (1.5 mm). The hydrochloride had m. p. 229-230° (decomp.) (from anhydrous alcohol).

Found %: N 6.32; Cl 15.4.  $C_{11}H_{15}O_2N \cdot HCl$ . Calculated %: N 6.10; Cl 15.43.

1-Bis(β-hydroxyethyl)-aminoindans and 1-bis(β-chloroethyl)-aminoindans. 1-Bis(β-hydroxyethyl)-aminoindans were obtained from 0.055 mole of the appropriate 1-aminoindan and 0.11 mole of ethylene oxide by heating in a sealed tube at 130-140° for 5-6 hr. The compounds obtained were uncrystallizable oils which could not be vacuum distilled. Some of them were isolated as hydrochlorides.

1-Bis(β-chloroethyl)-aminoindans were obtained from the corresponding 1-bis(hydroxyethyl)aminoindans by the action of thionyl chloride.

1-Bis(β-hydroxyethyl)-aminoindan. This compound was a thick, dark red oil with b. p. 184-190° (2 mm). The substance was not purified further. The yield was 73%.

1-Bis(β-chloroethyl)-aminoindan hydrochloride. To 2 g of 1-bis(β-hydroxyethyl)-aminoindan in 30 ml of dry chloroform was added 5 ml of freshly distilled thionyl chloride at -5 to 0°. The mixture was left at room temperature overnight. We isolated 2.5 g (94.7%) of the hydrochloride with m. p. 144-146° and after recrystallization from ethyl acetate, the substance had m. p. 155-155.5°.

Found %: C 52.97; H 5.91; N 4.63; Cl 36.44.  $C_{13}H_{17}NCl_2 \cdot HCl$ . Calculated %: C 52.98; H 6.15; N 4.76; Cl 36.19.

3-Carbethoxy-1-bis(β-chloroethyl)-1-aminoindan hydrochloride. This compound was obtained analogously from 16 g of undistilled 3-carbethoxy-1-bis(β-hydroxyethyl)-aminoindan and 15 ml of thionyl chloride. The hydrochloride isolated was purified through the base. After repeated recrystallization from benzene and a few drops of alcohol, the substance had m. p. 172-174.5°.

Found %: C 52.46; H 6.02; N 3.59; Cl 29.05.  $C_{16}H_{21}O_2NCl_2 \cdot HCl$ . Calculated %: C 52.40; H 6.04; N 3.82; Cl 29.00.

3-Carboxy-1-bis(β-chloroethyl)-aminoindan hydrochloride. A mixture of 0.5 g of 3-carbethoxy-bis(β-chloroethyl)-aminoindan hydrochloride and 2.5 ml of concentrated hydrochloric acid was heated at 100° for 1 hr. The water was removed and the residue purified by solution in acetone and precipitation with ether. The material was dried for 2 days over phosphorus pentoxide in a vacuum desiccator. The substance was hygroscopic. It had m. p. 45-50° (decomp.).

\* This amine was obtained by reduction of the corresponding oxime with sodium amalgam [1].

Found %: C 49.80; H 5.38; N 4.18; Cl (ionic) 10.40.  $C_{14}H_{17}O_2NCl_2 \cdot HCl$ . Calculated %: C 49.64; H 5.35; N 4.14; Cl (ionic) 10.47.

5-Methoxy-1-bis( $\beta$ -hydroxyethyl)-aminoindan. The substance had m. p. 89-91°.

Found %: C 66.24; H 8.39; N 5.78; OH 13.61.  $C_{14}H_{21}O_3N$ . Calculated %: C 67.00; H 8.34; N 5.56; OH 13.56.

5-Methoxy-1-bis( $\beta$ -hydroxyethyl)-aminoindan hydrochloride. The m. p. was 122-124°.

Found %: C 58.42; H 7.58; N 4.85; Cl 12.20.  $C_{14}H_{21}O_3N \cdot HCl$ . Calculated %: C 58.40; H 7.65; N 4.86; Cl 12.38.

5,6-Dimethoxy-bis( $\beta$ -hydroxyethyl)-1-aminoindan hydrochloride. The m. p. was 142-144° (from anhydrous alcohol).

Found %: C 56.89; H 7.49; N 4.46; Cl 10.95; 10.92.  $C_{15}H_{23}O_4N \cdot HCl$ . Calculated %: C 56.68; H 7.61; N 4.42; Cl 11.12.

6-Methoxy-1-bis( $\beta$ -chloroethyl)-aminoindan hydrochloride. This compound was obtained in the usual way from 4 g of distilled 6-methoxy-1-bis( $\beta$ -hydroxyethyl)-aminoindan and 8 ml of thionyl chloride. The dark oily substance which remained after removal of the solvent and excess thionyl chloride solidified when triturated with absolute ether. The hydrochloride was purified through the base. It was recrystallized from a mixture of ethyl acetate and alcohol. It had m. p. 168-169.5°.

Found %: C 51.98, 51.81; H 6.27, 6.32; N 4.25, 4.39; Cl 32.82.  $C_{14}H_{19}ONCl_2 \cdot HCl$ . Calculated %: C 51.98; H 6.18; N 4.32; Cl 32.90.

#### SUMMARY

1. Cyclization of aliphatic-aromatic acids or their acid chlorides yielded some 1-indanones with substituents in the aromatic or alicyclic parts of the indan ring.
2. The oximes of the 1-indanones obtained were reduced to the corresponding 1-aminoindans.
3. Bis- $\beta$ -chloroethyl derivatives of 1-aminoindan, 3-carboxy-1-aminoindan, 3-carbethoxy-1-aminoindan, and 6-methoxy-1-aminoindan were prepared. It was found that the C-N bond in bis- $\beta$ -chloroethyl derivatives of 5-methoxy- and 5,6-dimethoxy-1-aminoindans is unstable.

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# REACTION OF PIRYLOCYANINES WITH COMPOUNDS CONTAINING ACTIVE METHYL OR METHYLENE GROUPS

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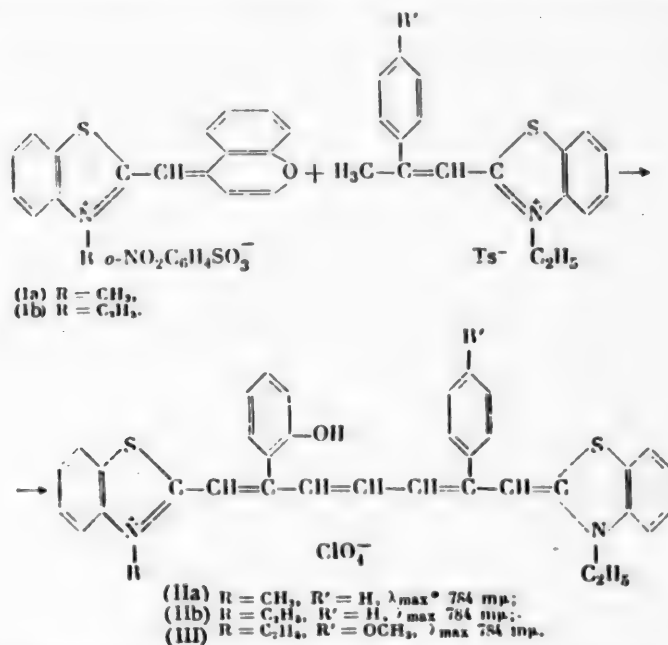
November, 1960

Original article submitted November 20, 1959

In a previous communication [1] we described the reaction between monomethynecyanines of type (I) and quaternary salts of nitrogen heterocycles with active methyl groups. It was found that this reaction yields dicarbocyanines containing *o*-hydroxyphenyl groups as substituents in the polymethyne chain.

In the present work it was shown that pyrylocyanines may react not only with quaternary salts of nitrogen heterocycles with active methyl groups in the heterocyclic nuclei, but also with more complex compounds containing active methyl groups. Compounds with active methylene groups can also react with pyrylocyanines.

Monomethynecyanines of type (I) react readily with quaternary salts of 2-( $\beta$ -aryl)propenylbenzthiazole. The reaction forms tricarbecyanines containing two aromatic nuclei as substituents in the chromophore.

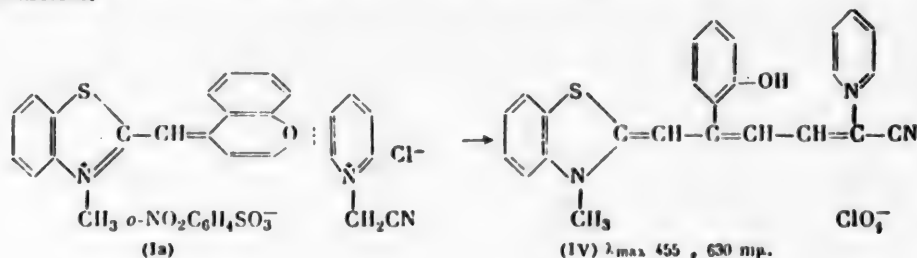


The reaction was carried out in methanol in the presence of anhydrous sodium acetate. The dyes were formed in yields of 30-50%.

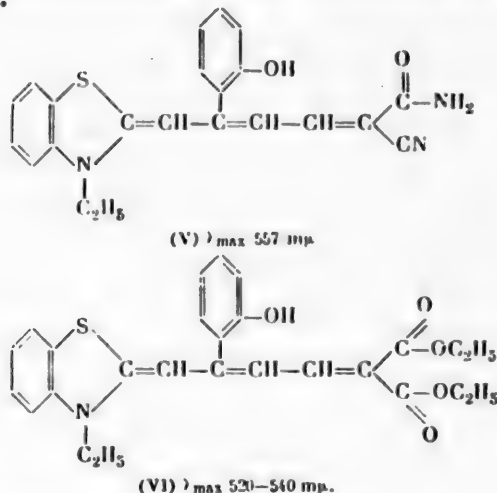
\*Here and elsewhere the values of  $\lambda_{\max}$  are given for alcohol solutions.

The absorption maxima of the thiatricarbocyanines (IIb) and (III) coincided and were displaced toward longer wavelengths by 22 m $\mu$  in comparison with the absorption maximum of the thiatricarbocyanine without substituents in the chromophore (which has  $\lambda_{\max}$  762 m $\mu$  [2]). This means that the introduction of a substituent such as a methoxyl group into a phenyl ring in the chromophore does not affect the absorption spectrum of the thiatricarbocyanine. As in the case of the similar dicarbocyanines, a change from a phenol to a phenolate group in the dyes examined produced a hypsochromic displacement of the absorption maximum [the dye (IIb) had  $\lambda_{\max}$  770 m $\mu$  in the presence of alcoholic alkali]. This phenomenon must be explained in the same way as for dicarbocyanines with a *o*-hydroxyphenyl substituent in the chromophore [1].

Substances containing active methylene groups reacted with monomethynecyanines of type (I) analogously to compounds with active methyl groups. For example, the following reaction occurred with *N*-cyanomethylpyridinium chloride:

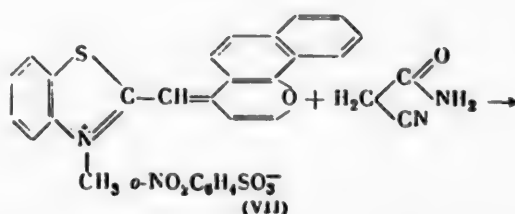


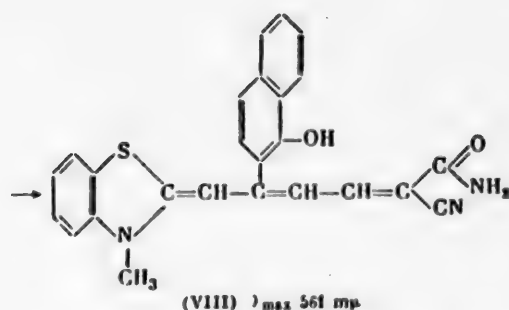
The reaction of the monomethynecyanine (Ib) with cyanoacetamide and malonic ester yielded the condensation products (V) and (VI).



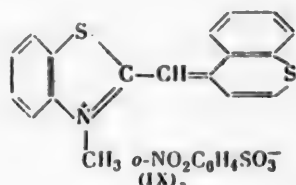
Compounds (V) and (VI) absorbed at shorter wavelengths with a change to less polar solvents [for (V)  $\lambda_{\max}$  in benzene was 544 m $\mu$ , and for (VI) the corresponding value was 494 m $\mu$ ].

Monomethynecyanines containing  $\alpha$ -naphthopyrillium nuclei (VII) reacted analogously with compounds containing active methylene groups:

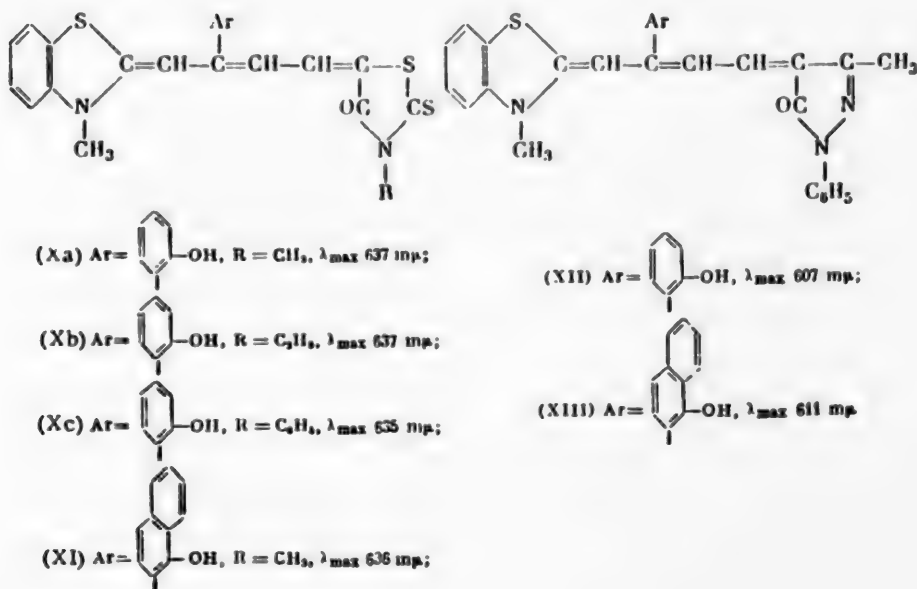




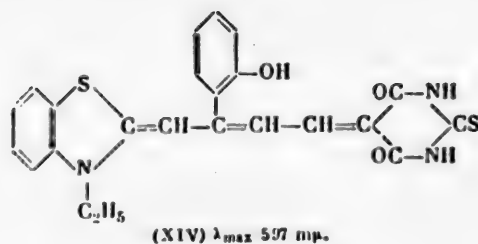
Thiopyrylocyanines were cleaved with much more difficulty. When the monomethynecyanine (IX) was heated with compounds containing active methylene groups in a mixture of acetic anhydride and pyridine, colors appeared which were characteristic of the reaction products. However, it was impossible to isolate them in an analytically pure state.



The use of heterocyclic compounds as substances with active methylene groups in this reaction deserves particular attention. The condensation of compounds (Ia) and (VII) with N-alkylrhodanines and 1-phenyl-3-methyl-5-pyrazolone and also substance (Ib) with thiobarbituric acid yielded compounds (X)-(XIV), which are tetramethynemerocyanines containing o-hydroxyphenyl or 1-hydroxy-2-naphthyl substituents in the chromophore.





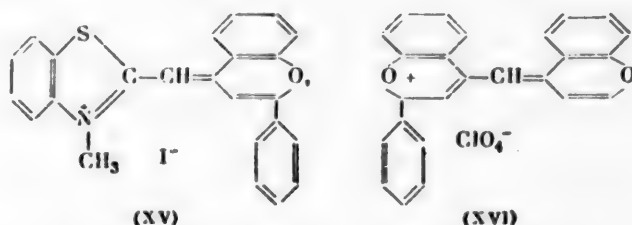


A comparison of the absorption maxima of the merocyanines (Xa) and (XI) shows that the nature of the aryl substituents does not appreciably affect the absorption maxima of these dyes. Hence, it may be concluded that the aryl substituents in these compounds lie perpendicular to the plane of the dye molecule. As in the case of 9-*o*-hydroxyphenylthiacarbocyanine [3], the color of these compounds did not change in the presence of alkali.

The reaction between pyrylium salts and the compounds with active methylene groups was carried out in methanol or ethanol in the presence of anhydrous sodium acetate. The merocyanines (X)-(XIV) were formed particularly readily. The dyes were obtained in quantitative yields in the cold. In cases where the condensation was carried out with compounds of acyclic structure, the reaction proceeded much less smoothly and was often accompanied by the formation of by-products (as a spectroscopic study of di- and tricarbocyanines with *o*-hydroxyphenyl substituents in the chromophore showed). The pyrylium salts did not react under the given conditions with less active compounds [4] (benzyl cyanide, phenylacetic acid, etc.).

On the basis of the material presented in this and previous work [1] it must be concluded that pyrylium salts of type (I) react with compounds containing active methyl or methylene groups in a manner which differs fundamentally from that in which flavylium salts react [5]. The reaction described involves opening of the benzopyrylium ring, and in this respect it is more similar to the reactions of pyrylium salts with nucleophilic agents [6].

In conclusion, it should be emphasized that monomethynecyanines containing benzopyrylium nuclei may react with nucleophilic agents only if these nuclei do not contain aryl groups in position 2. For example, the flavylomonomethynecyanine (XV)



was found to be inert toward all the nucleophilic agents we tested. This is supported by the fact that the reaction of (4-flavylo)-(4'-benzopyrylo)-monomethynecyanine perchlorate (XVI) with 2-methylbenzthiazole ethotosylate forms a flavylthiadibocyanine [1] and not a polymethyne dye with a longer chain, i.e., the flavylium nucleus is not touched in this case.

## EXPERIMENTAL

(3-Methylbenzthiazole-2)-(3'-ethylbenzthiazole-2')-9-(*o*-hydroxyphenyl)-13-phenyltricarbocyanine perchlorate (IIa). A mixture of 0.245 g of 2-[( $\gamma$ -benzopyranilidene)-methyl]-benzthiazole metho-*o*-nitrobenzenesulfonate (Ia) [7] and 0.255 g of 8-phenylpropenylbenzthiazole ethiodide [3] was dissolved in 40 ml of hot methanol, the solution filtered and 0.05 g of anhydrous sodium acetate added to it, and heating continued for a further 30 min. To the cooled solution was added 10 ml of an aqueous solution of potassium iodide. After the solution had been kept for 4-5 hr, the dye liberated was collected and washed on the filter with alcohol, water, and again alcohol. We obtained 0.12 g (34%) of the substance. The green, lustrous leaflets had *m. p.* 188°.

Found %: I 17.85, 17.91.  $C_{36}H_{31}ON_2S_2I$ . Calculated %: I 18.19.

The dye was converted to the perchlorate by adding a methanol solution of sodium perchlorate to a methanol solution of the dye. The green, lustrous crystals had m. p. 189°.

Found %: S 9.45, 9.52.  $C_{36}H_{31}O_5N_2S_2Cl$ . Calculated %: S 9.54.

3,3'-Diethyl-9-(o-hydroxyphenyl)-13-phenylthiatricarbocyanine perchlorate (IIb). A mixture of 0.51 g of 2-[ $\gamma$ -benzopyranylidene]-methyl]-benzthiazole etho-o-nitrobenzenesulfonate (Ib) [7], 0.45 g of 8-phenylpropenylbenzthiazole ethiodide, and 0.1 g of anhydrous sodium acetate in 45 ml of anhydrous methanol was boiled for 40 min on a water bath. To the cooled solution was added 10 ml of an aqueous solution of potassium iodide. The dye which had precipitated after the solution had stood for 3 hours was collected and washed on the filter successively with methanol, water, methanol, and ether. We obtained 0.35 g (50%) of the substance. The fine green leaflets had m. p. 192°. The dye was converted to the perchlorate by adding a methanol solution of sodium perchlorate to a methanol solution of the dye. The lustrous green needles had m. p. 207°.

Found %: S 9.27, 9.37.  $C_{37}H_{33}O_5N_2S_2Cl$ . Calculated %: S 9.35.

3,3'-Diethyl-9-(o-hydroxyphenyl)-13-(p-methoxyphenyl)-thiatricarbocyanine perchlorate (III). A mixture of 0.254 g of the monomethynecyanine (Ib) and 0.24 g of 2-8-(p-methoxyphenyl)-propenylbenzthiazole ethotosylate [3] was dissolved in 20 ml of hot anhydrous methanol and then 0.05 g of anhydrous sodium acetate added and the solution left at room temperature for 24 hr. To the solution was added 3 ml of an aqueous solution of potassium iodide and the mixture left overnight. The precipitated dye was collected and washed on the filter with several drops of methanol and water. We obtained 0.1 g (27%) of the dye. The lustrous green leaflets had m. p. 179°.

Found %: I 16.81, 16.65.  $C_{33}H_{25}O_2N_2S_2I$ . Calculated %: I 17.12.

N-[5-(3'-Methylbenzthiazolinyldene-2')-4-(o-hydroxyphenyl)-1-cyanopenta-1,3-dien-1-yl]-pyridinium perchlorate (IV). A mixture of 0.494 g of the monomethynecyanine (Ia), 0.19 g of N-cyanomethylpyridinium chloride [8], 0.1 g of anhydrous sodium acetate, and 5 ml of anhydrous ethanol was heated for 3 min. The oily product which precipitated when the cooled mixture was diluted with ether was washed with ether by decantation. The substance was converted to the perchlorate by treating a methanol solution of it with an aqueous solution of sodium perchlorate. Recrystallization from ethanol yielded 0.34 g (66.5%) of a dark blue substance with a metallic luster.

Found %: N 7.90, 8.01.  $C_{25}H_{20}O_5N_3SCl$ . Calculated %: N 8.24.

1-(3'-Ethylbenzthiazolinyldene-2')-2-(o-hydroxyphenyl)-5-cyano-5-carbamidopenta-2,4-diene (V). A mixture of 1.02 g of the pyriocyanine (Ib), 0.2 g of cyanoacetamide, 0.2 g of anhydrous sodium acetate, and 10 ml of anhydrous ethanol was heated for 3 min. The precipitated product was collected, washed on the filter with water, and recrystallized twice from alcohol. We obtained 0.49 g (63%) of the substance. The black prisms with a metallic luster had m. p. 215°.

Found %: N 10.49, 10.57.  $C_{22}H_{19}O_2N_3S$ . Calculated %: N 10.80.

1-(3'-Ethylbenzthiazolinyldene-2')-2-(o-hydroxyphenyl)-5,5-dicarbethoxypenta-2,4-diene (VI). A mixture of 0.51 g of the monomethynecyanine (Ib), 1 ml of malonic ester, 0.1 g of anhydrous sodium acetate, and 50 ml of anhydrous methanol was heated for 10 min. Half of the methanol was then removed on a water bath and the residue diluted with water. The precipitated product was collected and chromatographed in chloroform on alumina. The middle, brown zone was separated mechanically. When the methanol eluate obtained from this zone was cooled in ice water the dye separated. Recrystallization from ethanol yielded 0.1 g (21%) of substance. The lustrous orange leaflets had m. p. 174°.

Found %: S 6.92, 6.93.  $C_{26}H_{27}O_5NS$ . Calculated %: S 6.88.

1-(3'-Methylbenzthiazolinyldene-2')-2-(1'-hydroxynaphthyl-2'')-5-cyano-5-carbamidopenta-2,4-diene (VIII). A mixture of 0.558 g of the monomethynecyanine (VII) [7], 0.1 g of cyanoacetamide, 0.1 g of anhydrous sodium acetate, and 5 ml of anhydrous ethanol was heated for 5 min. The precipitated product was collected by filtration. Recrystallization from xylene yielded 0.24 g (56.5%) of substance. The black needles with a bronze luster had m. p. 195°.

Found %: N 9.26, 9.24.  $C_{26}H_{21}O_2N_2S$ . Calculated %: N 9.57.

3-Methyl-5-[1'-(3'-methylbenzthiazolinyldene-2'')-2'-(o-hydroxyphenyl)-butenyldene-4'']-thiazolidene-2-thion-4-one (Xa). A mixture of 0.388 g of the monomethynecyanine (Ia) and 0.37 g of 3-methylrhodanine was dissolved in 200 ml of hot anhydrous methanol. The solution was filtered and 0.2 g of anhydrous sodium acetate added. After the mixture had been kept at room temperature for 4 hr, the precipitated dye was collected and washed on the filter with hot methanol. We obtained 0.83 g (98.5%) of substance. The green leaflets had m. p. 221-222°.

Found %: S 22.17, 22.07.  $C_{22}H_{16}O_2N_2S_3$ . Calculated %: S 21.92.

The tetramethynemerocyanine (Xb) was obtained from the monomethynecyanine (Ia) and 3-ethylrhodanine analogously to the previous compound. The yield was 93%. The lustrous green leaflets had m. p. 235-236°.

Found %: S 21.39, 21.21.  $C_{23}H_{20}O_2N_2S_3$ . Calculated %: S 21.24.

The tetramethynemerocyanine (Xc) was obtained from the monomethynecyanine (Ia) and 3-phenylrhodanine analogously to the tetramethynemerocyanine (Xa). The yield was 70%.

The lustrous blue-green platelets had m. p. 217-218°.

Found %: S 18.87, 19.18.  $C_{27}H_{20}O_2N_2S_3$ . Calculated %: S 19.20.

3-Methyl-5-[1'-(3'-methylbenzthiazolinyldene-2'')-2-(1''-hydroxynaphthyl-2'')-butenyldene-4'']-thiazolidine-2-thion-4-one (XI). A mixture of 0.27 g of the monomethynecyanine (VII) [7], 0.088 g of 3-methylrhodanine, 0.05 g of anhydrous sodium acetate, and 50 ml of anhydrous methanol was heated for 5 min. The dye was collected and washed on the filter with methanol. We obtained 0.225 g (92.5%) of substance. On recrystallization from nitromethane, the product formed dark blue platelets with a green iridescence and with dec. p. 228°.

Found %: S 19.50, 19.59.  $C_{26}H_{20}O_2N_2S_3$ . Calculated %: S 19.67.

1-Phenyl-3-methyl-4-[1'-(3'-methylbenzthiazolinyldene-2'')-2'-(o-hydroxyphenyl)-butenyldene-4'']-pyrazolid-5-one (XII). A mixture of 0.494 g of the monomethynecyanine (Ia), 0.226 g of 1-phenyl-3-methyl-5-pyrazolone, 0.1 g of anhydrous sodium acetate, and 10 ml of anhydrous ethanol was heated for 5 min. The dye was collected and washed on the filter with ethanol and water. Recrystallization from benzene yielded 0.42 g (90%) of substance. The fine blue needles had m. p. 231°.

Found %: N 8.80, 8.85.  $C_{28}H_{23}O_2N_3S$ . Calculated %: N 9.03.

The tetramethynemerocyanine (XII) was obtained from the monomethynecyanine (VII) and 1-phenyl-3-methylpyrazolone analogously to the previous compound. The yield was 96%. Recrystallization from nitromethane gave dark green platelets with dec. p. 220°.

Found %: N 8.03, 7.86.  $C_{32}H_{25}O_2N_3S$ . Calculated %: N 8.16.

5-[1'-(3'-ethylbenzthiazolinyldene-2'')-2'-(o-hydroxyphenyl)-butenyldene-4'']-2-thiobarbituric acid (XIV). A mixture of 0.51 g of the monomethynecyanine (Ib) and 0.173 g of thiobarbituric acid was dissolved in 50 ml of hot anhydrous methanol, the solution filtered, and 0.2 g of anhydrous sodium acetate added. After being heated for 3 min, the mixture was left at room temperature for 2 hr. The precipitated product was collected and washed on the filter with methanol, water, methanol again, and ether. We obtained 0.38 g (84.5%) of dye. The dark blue crystals had dec. p. 315°.

Found %: S 14.20, 14.31.  $C_{23}H_{19}O_3N_3S_2$ . Calculated %: S 14.25.

## SUMMARY

1. It was shown that during the reaction of monomethynecyanines containing 4-benzopyrylium residues with quaternary salts of 2-(8-aryl)-propenylbenzthiazole there is cleavage of the benzopyrylium ring to form tricarbocyanines with o-hydroxyphenyl groups as substituents in the chromophore.

2. The reaction of monomethynecyanine containing 4-benzopyrylium nuclei with compounds containing active methylene groups was studied. It was shown that this reaction may be used to prepare tetramethynemerocyanines with o-hydroxyphenyl groups as substituents in the chromophore.

3. An analogous reaction occurs with monomethynecyanines containing 4- $\alpha$ -naphthopyryllum residues.
4. The absorption spectra of the dyes obtained were studied.

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# ADDITIONS TO SALTS OF PHENYLACETYLENYLPYRIDINES

A. I. Kiprianov and G. G. Dyadyusha

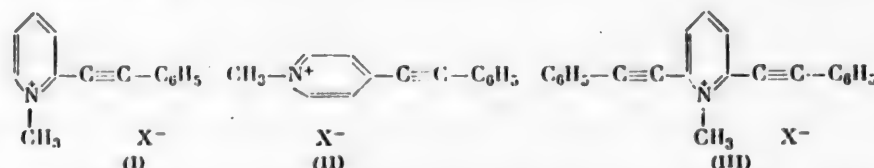
Institute of Organic Chemistry, Academy of Sciences, Ukr.SSR

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November, 1960

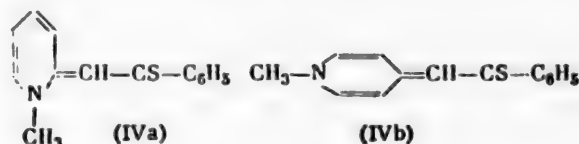
Original article submitted December 11, 1959

Continuing the investigation of additions to a triple bond conjugated with a negative heterocyclic residue [1], we synthesized N-methyl-2-phenylacetylenylpyridinium (I), N-methyl-4-phenylacetylenylpyridinium (II), and N-methyl-2,6-bis(phenylacetylenyl)pyridinium salts (III) by methylation of the bases, which have been described in literature [2-5].

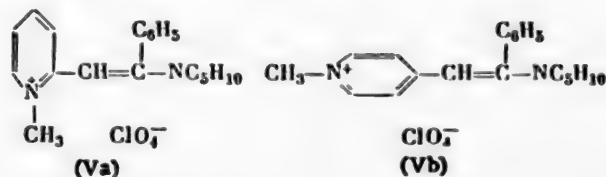


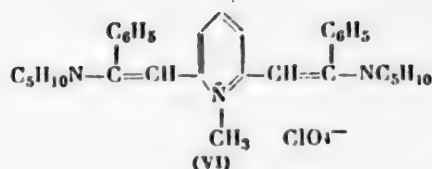
The ultraviolet spectra of 2-phenylacetylenylpyridinium and especially 2,6-bis(phenylacetylenyl)pyridinium quaternary salts showed a bathochromic displacement of the absorption maxima in comparison with the corresponding styryl derivatives. On the other hand, the replacement of the double bond by a triple bond in the 4-derivatives produced a hypsochromic displacement of the maximum.

Like quaternary salts of 2-phenylacetylenylquinoline [1], their pyridine analogs were capable of adding various nucleophilic reagents. The action of sodium hydrosulfide on the methosulfates of N-methyl-2- and 4-phenylacetylenylpyridines yielded yellow N-methylthiobenzoylmethylenedihydropyridines (IVa and IVb).

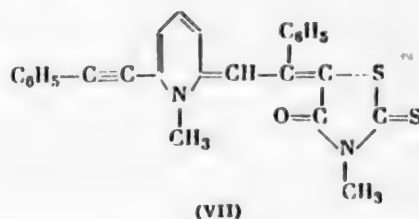


Treatment of alcohol solutions of the perchlorates of (I) and (II) with piperidine yielded the crystalline addition products (Va) and (Vb). Under the same conditions, N-methyl-2,6-bis(phenylacetylenyl)pyridinium perchlorate (III) added two molecules of piperidine to form the product (VI).





Merocyanines, derivatives of N-methylrhodanine, were obtained with the usual ease by the action of triethylamine on an alcohol solution of N-methylrhodanine and a phenylacetylenylpyridine quaternary salt. Under these conditions N-methyl-2,6-bis(phenylacetylenyl)pyridinium perchlorate condensed with only one molecule of N-methylrhodanine to form the dye (VII).



The structure of this dye was confirmed by the fact that its infrared spectrum contained a band with a frequency of  $2223\text{ cm}^{-1}$ , which is characteristic of monophenylacetylenylpyridines.

Phenylacetylenylpyridine quaternary salts underwent the carbocyanine condensation with much more difficulty than N-methyl-2-phenylacetylenylquinolinium salts. For the synthesis of unsymmetrical mesophenyl pyridocarbocyanines, it was necessary to boil the salt (I), (II) or (III) in alcohol with triethylamine and the quaternary salt containing the active methyl group, while in the case of heterocycles of lower basicity, for example trimethylindolenine, the condensation had to be carried out in boiling acetic anhydride. Despite the fact that the salt (III) formed intensely colored products under these conditions, we were unable to isolate individual dyes from them. Similarly, we did not isolate mesophenyl-4,4'-pyridocarbocyanine in a pure form, although the absorption curve of the reaction product in alcohol solution made it possible to assign to it reliably an absorption maximum of  $608\text{ m}\mu$ .

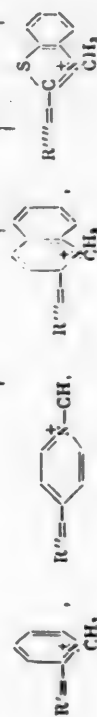
The absorption maxima and intensities and also the deviations ( $\Delta$ ) for unsymmetrical dyes and displacements of the absorption maxima ( $\delta$ ) as a result of replacement of a hydrogen atom in a meso position by a phenyl group for alcohol solutions of the dyes we synthesized are given in the table. The unsymmetrical pyridocarbocyanines not containing phenyl radicals which are given in the table were prepared by condensation of anilido- or acetanilidovinyl derivatives of N-methylquinolinium, N-methylbenzthiazolium, and N-methylindoleninium with methiodides of  $\alpha$ - and  $\gamma$ -picolines [6].

A comparison of the absorption maxima of the dyes given in the table shows that the introduction of a phenyl group into 2,2'-pyridocarbocyanine (VIII) disrupts the coplanarity of the heterocyclic nuclei due to steric hindrance as with isosteric 2,2'-quinocarbocyanine (XII) [1, 12, 13]. On the other hand, in the molecule of mesophenyl-4,4'-pyridocarbocyanine (XXI), the absence of a methyl group in close proximity to the polymethyne chain allows the heterocycles to remain coplanar or almost coplanar. In this case there is a small bathochromic displacement as in the case of mesophenylthiocarbocyanine (XXVII). For the unsymmetrical dyes (XXII) and (XXIV), with nuclei which are very different in basicity, the bathochromic displacements ( $\delta$ ) produced by the introduction of a phenyl group were found to be comparatively small. In the chains of these dyes the bonds are already of different orders, and the rotation of the nuclei occurs through bonds of low order. Disruption of the coplanarity of the nuclei of an unsymmetrical dye increases the deviation and reduces the molar extinction coefficient. For the unsymmetrical mesophenylpyridothiocarbocyanine (XXV), the pyridine and benzthiazole nuclei retain their coplanarity and the values of the deviation and molecular extinction remain unchanged in comparison with the unsubstituted dye (XIV).

For the pyridindocarbocyanines (XVII) and (XVIII) the deviations are very large. The heterocycles of these dyes differ sharply in basicity. The bonds in their chains are no longer equalized and approach alternating



Dye	R=H				R=C <sub>6</sub> H <sub>5</sub>						
	X	No.	$\lambda_{\max}$ (m $\mu$ )	lg $\epsilon$	$\Delta$ (m $\mu$ )	X	No.	$\lambda_{\max}$ (m $\mu$ )	lg $\epsilon$	$\Delta$ (m $\mu$ )	$\delta$ (m $\mu$ )
	I	VIII	559a			ClO <sub>4</sub>	XX	606	4.30		47
	ClO <sub>4</sub>	IX	605b			ClO <sub>4</sub>	XXI	608			3
	I	X	577	4.96	5	ClO <sub>4</sub>	XXII	594	4.27	33	17
	I	XI	597	4.99	8	I	XXIII	648 [1]	4.84		43
	I	XII	605c	5.28							
	I	XIII	536	4.94	22.5	ClO <sub>4</sub>	XXIV	544	4.74	39	8
	I	XIV	557	4.98	24.5	ClO <sub>4</sub>	XXV	561	5.01	23	4
	CH <sub>3</sub> SO <sub>4</sub>	XV	582d		-0.5	ClO <sub>4</sub>	XXVI	603 [1]	5.00	1	21
	I	XVI	558 [10]			ClO <sub>4</sub>	XXVII	560 [11]			2
	I	XVII	509	4.88	43	ClO <sub>4</sub>	XXVIII	460	3.79		-49
	I	XVIII	525	4.99	50	ClO <sub>4</sub>	XXIX	473	4.08		-52
	ClO <sub>4</sub>	XIX	550 [10]		25	ClO <sub>4</sub>	XXX	596 [1]	4.60		46



<sup>a</sup> In methanol  $\lambda_{\max}$  558 m $\mu$  [7].

b Iodide of the N,N'-diethyl derivative in methanol  $\lambda_{\max}$  603 m $\mu$  [8].

c In methanol  $\lambda_{\max}$  604 m $\mu$  [9].

d Iodide of the N,N'-diethyl derivative in methanol  $\lambda_{\max}$  578 m $\mu$  [9].

single and double bonds. The introduction of a phenyl into the meso position (dyes XXV/III and XXIX) here leads to the rotation of the heterocycles about the bonds which are almost single. This results in not bathochromic, but strong hypsochromic displacements of the maxima  $\delta$ . At the same time, the introduction of phenyl groups produces a decrease in absorption intensity by a factor of almost ten.

#### EXPERIMENTAL

2-Phenylacetylenylpyridine was obtained by the method in [2]. We were able to crystallize this preparation, which was described as a liquid, by cooling it to low temperature (ether and solid carbon dioxide). The hexagonal tablets had m. p. 32.5°. The infrared spectrum had a triple bond band at 2226  $\text{cm}^{-1}$ .

Found %: N 7.68, 7.72.  $\text{C}_{13}\text{H}_9\text{N}$ . Calculated %: N 7.82.

4-Phenylacetylenylpyridine [3] had m. p. 101-103° (102-104° [5]). The infrared spectrum of a  $\text{CCl}_4$  solution had a band at 2225  $\text{cm}^{-1}$ .

2,6-bis(phenylacetylenylpyridine) [2] had m. p. 137-138°. The infrared spectrum had a band at 2217  $\text{cm}^{-1}$ .

The N-methyl methosulfates were obtained by the action of dimethyl sulfate in benzene on the above bases. The perchlorates were prepared by precipitation with a methanol solution of sodium perchlorate from methanol solutions of the methosulfates.

N-Methyl-2-phenylacetylenylpyridinium methosulfate was purified by solution in chloroform and precipitation with acetone. It formed prisms with m. p. 111-112°.

N-Methyl-2-phenylacetylenylpyridinium perchlorate formed oblique tablets with m. p. 156-157°.

Ultraviolet spectrum (in alcohol):  $\lambda_{\text{max}}$  336.5, 259 and 224  $\text{m}\mu$  ( $\log \epsilon$  4.47, 4.14 and 4.40). Found %: Cl 12.14, 12.22.  $\text{C}_{14}\text{H}_{12}\text{O}_4\text{NCl}$ . Calculated %: Cl 12.07.

N-Methyl-4-phenylacetylenylpyridinium methosulfate formed prisms with m. p. 183° after recrystallization from alcohol.

Ultraviolet spectrum:  $\lambda_{\text{max}}$  336, 281 and 235  $\text{m}\mu$  ( $\log \epsilon$  4.41, 3.93 and 4.05). Found %: S 10.53, 10.36.  $\text{C}_{15}\text{H}_{15}\text{O}_4\text{NS}$ . Calculated %: S 10.50.

N-Methyl-4-phenylacetylenylpyridinium perchlorate formed needles with m. p. 158° (from methanol).

Found %: Cl 12.51, 12.46.  $\text{C}_{14}\text{H}_{12}\text{O}_4\text{NCl}$ . Calculated %: Cl 12.07.

N-Methyl-2,6-bis(phenylacetylenylpyridinium perchlorate) formed long needles with m. p. 226° (decomp., from alcohol).

Ultraviolet spectrum:  $\lambda_{\text{max}}$  374, 265-305, 224  $\text{m}\mu$  ( $\log \epsilon$  4.45, 4.20, 4.44). Found %: Cl 9.04, 9.14.  $\text{C}_{22}\text{H}_{16}\text{O}_4\text{NCl}$ . Calculated %: Cl 9.00.

The following salts were obtained analogously from styrylpyridines.

N-Methyl-2-styrylpyridinium perchlorate formed prisms with m. p. 178° (from methanol).

Ultraviolet spectrum:  $\lambda_{\text{max}}$  332, 263  $\text{m}\mu$  ( $\log \epsilon$  4.15, 3.77). Found %: Cl 12.02, 12.06.  $\text{C}_{14}\text{H}_{14}\text{O}_4\text{NCl}$ . Calculated %: Cl 11.99.

N-Methyl-4-styrylpyridinium methosulfate formed prisms with m. p. 184-185° (from methanol).

Ultraviolet spectrum:  $\lambda_{\text{max}}$  345, 242  $\text{m}\mu$  ( $\log \epsilon$  4.41, 4.00). Found %: S 10.28, 10.34.  $\text{C}_{15}\text{H}_{17}\text{O}_4\text{NS}$ . Calculated %: S 10.43.

N-Methyl-2,6-bis(styryl)pyridinium perchlorate formed yellow spherical aggregates of crystals with m. p. 207° (from methanol).

Ultraviolet spectrum:  $\lambda_{\text{max}}$  349, 288, 208  $\text{m}\mu$  ( $\log \epsilon$  4.26, 4.28, 4.40). Found %: Cl 9.02, 9.17.  $\text{C}_{22}\text{H}_{20}\text{O}_4\text{NCl}$ . Calculated %: Cl 8.91.

N-Methyl-2-thiobenzoylmethylene-1,2-dihydropyridine (IVa). To a solution of 0.7 g of  $\text{Na}_2\text{S} \cdot 9\text{H}_2\text{O}$  in 3 ml of methanol was added a solution of 0.3 ml of concentrated hydrochloric acid in 3 ml of methanol and

then, with stirring, a solution of 0.5 g of the methosulfate (I) in 3 ml of methanol. The methanol was removed on a water bath, the residue diluted with water, and the precipitate recrystallized from methanol. The yield was 0.30 g (82%) of orange prisms with m. p. 166°.  $\lambda_{\max}$  461 m $\mu$  (log  $\epsilon$  4.27).

Found %: S 13.96, 14.06.  $C_{14}H_{13}NS$ . Calculated %: S 14.11.

N-Methyl-4-thiobenzoylmethylene-1,2-dihydropyridine (IVb) was obtained exactly as the previous preparation in 77% yield. The bright red octahedra had m. p. 212-213°.  $\lambda_{\max}$  468 m $\mu$  (log  $\epsilon$  4.48).

Found %: S 13.96, 14.01.  $C_{14}H_{13}NS$ . Calculated %: S 14.11.

N-Methyl-2-( $\alpha$ -piperidylstyryl)-pyridinium perchlorate (Va). To a suspension of 0.25 g of the perchlorate (I) in 2 ml of methanol was added 0.1 g of piperidine. The salt dissolved on heating, and when the solution cooled it deposited yellow tablets with m. p. 182-184°. The yield was 0.29 g (90%).  $\lambda_{\max}$  406 m $\mu$  (log  $\epsilon$  4.50).

Found %: N 7.38, 7.48.  $C_{19}H_{23}O_4N_2Cl$ . Calculated %: N 7.40.

N-Methyl-4-( $\alpha$ -piperidylstyryl)-pyridinium perchlorate (Vb) was obtained in exactly the same way as the previous compound. The light yellow prisms had m. p. 134-135°.  $\lambda_{\max}$  412 m $\mu$  (log  $\epsilon$  4.75).

Found %: N 7.14, 7.29.  $C_{19}H_{23}O_4N_2Cl$ . Calculated %: N 7.40.

N-Methyl-2,6-bis( $\alpha$ -piperidylstyryl)-pyridinium perchlorate (VI) was obtained by the same method. The light yellow prisms had m. p. 210-211°.  $\lambda_{\max}$  452 m $\mu$  (log  $\epsilon$  4.61).

Found %: N 7.29, 7.40.  $C_{32}H_{38}O_4N_3Cl$ . Calculated %: N 7.45.

3-Methyl-5-[ $\alpha$ -phenyl- $\beta$ -(1'-methyl-2'-ethyldihydropyridylidene-2')-ethyldiene]-rhodanine. To a solution of 0.5 g of the methosulfate (I) and 0.23 ml of triethylamine was added 0.26 g of N-methylrhodanine in 2 ml of alcohol. The precipitate was recrystallized from alcohol. The black prisms had m. p. 227°. The yield was 0.36 g (64%). In alcohol  $\lambda_{\max}$  559 m $\mu$  and in chloroform 577 m $\mu$  (log  $\epsilon$  4.77).

Found %: S 18.45, 18.64.  $C_{18}H_{16}ON_2S_2$ . Calculated %: S 18.84.

3-Methyl-5-[ $\alpha$ -phenyl- $\beta$ -(1'-methyl-2'-ethyldihydropyridylidene-4')-ethyldiene]-rhodanine was obtained analogously. The dark prisms with a bronze luster had m. p. 248°; the yield was 44%. In alcohol,  $\lambda_{\max}$  578 m $\mu$  and in chloroform 595 m $\mu$  (log  $\epsilon$  4.62).

Found %: S 18.94, 18.99.  $C_{18}H_{16}ON_2S_2$ . Calculated %: S 18.84.

3-Methyl-5-[ $\alpha$ -phenyl- $\beta$ -(1'-methyl-6'-phenylacetylenyldihydropyridylidene-2')-ethyldiene]-rhodanine (VII) was obtained as above from 0.5 g of the perchlorate (III), 0.3 g of N-methylrhodanine, and 0.2 ml of triethylamine in 10 ml of methanol. The preparation was purified by precipitation with methanol from chloroform solution. The dark prisms had m. p. 247-249°; the yield was 0.40 g (71%). In alcohol  $\lambda_{\max}$  581 m $\mu$  and in chloroform 586 m $\mu$  (log  $\epsilon$  4.58).

Found %: S 14.31, 14.26.  $C_{26}H_{20}ON_2S_2$ . Calculated %: S 14.56.

1,1'-Dimethyl-8-phenyl-2,2'-pyridocarbocyanine perchlorate (XX). A mixture of 0.5 g of the methosulfate (I), 0.5 g of  $\alpha$ -picoline methiodide, 0.23 ml of triethylamine, and 2 ml of alcohol was boiled for 15 min, and then a solution of 0.3 g of sodium perchlorate in 2 ml of water was added. The dye was washed with water and chromatographed in acetone on alumina. We obtained 0.117 g (18%) of prisms with a bronze luster and m. p. 226°.

Found %: N 6.81, 6.75.  $C_{21}H_{21}O_4N_2Cl$ . Calculated %: N 6.99.

1,3'-Dimethyl-8-phenyl-2-pyridothiocarbocyanine perchlorate (XXIV). This was obtained analogously to the previous dye. The black prisms had m. p. 228-229° (decomp.) and the yield was 4.5%.

Found %: Cl 7.78, 7.95.  $C_{23}H_{21}O_4N_2SCl$ . Calculated %: Cl 7.76.

1,1'-Dimethyl-8-phenyl-2-pyrido-2'-quinocarbocyanine perchlorate (XXII) was obtained by the same method. It was purified by a second recrystallization from methanol. The bronze leaflets had m. p. 192-193° and the yield was 32%.

Found %: Cl 8.05, 8.04.  $C_{25}H_{23}O_4N_2Cl$ . Calculated %: Cl 7.86.

1,1'-Dimethyl-8-phenyl-4-pyridocarbocyanine (XXI) was not obtained in a pure form. Under the conditions of the preparation of the previous dyes, an intense blue tarry precipitate was formed, and a freshly prepared alcohol solution of this had a single narrow absorption band in the visible part of the spectrum at 608 m $\mu$ .

1,3'-Dimethyl-8-phenyl-4-pyridothiocarbocyanine perchlorate (XXV). A mixture of 0.2 g of the methosulfate (II), 0.2 g of 2,3-dimethylbenzthiazolium methosulfate, 0.2 ml of triethylamine, and 1 ml of acetic anhydride was heated at 120° for 15 min. The dye was precipitated with ether, dissolved in water, and precipitated with sodium perchlorate. The precipitate was chromatographed in acetone on alumina and recrystallized twice from methanol. The red prisms with a green luster had m. p. 236-238° and the yield was 33 mg (11%).

Found %: Cl 7.69, 7.67.  $C_{23}H_{21}O_4N_2SCl$ . Calculated %: Cl 7.76.

1,1',3',3'-Tetramethyl-8-phenyl-2-pyridoincarbocyanine perchlorate (XXVIII). A mixture of 0.5 g of the methosulfate (I), 0.5 g of 2,3,3-trimethylindolenine methiodide, and 4 ml of acetic anhydride was treated as in the previous case. The dye was precipitated with sodium perchlorate. The yield of dark red prisms with m. p. 233-234° (decomp.) (from methanol) was 0.22 g (29%).

Found %: Cl 7.70, 7.68.  $C_{26}H_{27}O_4N_2Cl$ . Calculated %: Cl 7.59.

1,1',3',3'-Tetramethyl-8-phenyl-4-pyridoincarbocyanine perchlorate (XXIX) was obtained by the same method from the methosulfate (II). The yellow leaflets had m. p. 238-240° (decomp., from alcohol) and the yield was 48%.

Found %: Cl 7.42, 7.46.  $C_{26}H_{27}O_4N_2Cl$ . Calculated %: Cl 7.59.

1,1'-Dimethyl-2-pyrido-2'-quinocarbocyanine iodide (X). A mixture of 0.2 g of  $\alpha$ -picoline methiodide, 0.2 g of 2-anilino-1-vinylquinoline methiodide, 0.1 ml of triethylamine, and 1 ml of acetic anhydride was heated at 125° for 10 min. The dye was precipitated with ether and recrystallized from alcohol. The black crystalline powder had m. p. 240°. In alcohol  $\lambda_{max}$  542 m $\mu$  ( $\log \epsilon$  4.96, 4.88). Analogous dyes with ethyl groups at the nitrogen atoms have been described by Ogata [6] and Kotaki [14].

Found %: I 31.21, 31.37.  $C_{19}H_{19}N_2I$ . Calculated %: I 31.55.

1,1'-Dimethyl-4-pyrido-2'-quinocarbocyanine iodide (XI) was obtained in the same way as the previous one. It formed a crystalline powder with a bronze luster.

Ultraviolet spectrum (in alcohol):  $\lambda_{max}$  597, 559 m $\mu$  ( $\log \epsilon$  4.99, 4.87). Found %: I 31.16, 31.27.  $C_{19}H_{19}N_2I$ . Calculated %: I 31.55.

1,3'-Dimethyl-2-pyridothiocarbocyanine iodide (XIII) was obtained by the same method. The violet crystalline powder had m. p. 244°.

Found %: I 30.26, 30.28.  $C_{17}H_{17}N_2SI$ . Calculated %: I 31.08.

1,3'-Dimethyl-4-pyridothiocarbocyanine iodide (XIV). This was obtained by the same method. The violet needles had m. p. 253° (from alcohol) and the yield was 71%.

Found %: I 31.69, 31.79.  $C_{17}H_{17}N_2SI$ . Calculated %: I 31.08.

1,1',3',3'-Tetramethyl-2-pyridoincarbocyanine iodide (XVII). The dye was obtained by boiling a mixture of 0.5 g of  $\alpha$ -picoline methiodide, 0.5 g of 2-acetanilidovinyl-3,3-dimethylindolenine methiodide, 0.25 ml of triethylamine, and 2 ml of acetic anhydride; the yield was 0.28 g (38%) of dark red prisms with m. p. 249-250° (decomp., from alcohol). An analogous dye with an ethyl group at the nitrogen atom of the pyridine nucleus has been mentioned in the literature [15].

Found %: I 30.16, 30.07.  $C_{20}H_{23}N_2I$ . Calculated %: I 30.34.

1,1',3',3'-Tetramethyl-4-pyridoincarbocyanine iodide (XVIII) was obtained by the same method. The red crystals with a bronze luster had m. p. 285° (from alcohol) and the yield was 37%.

Found %: I 30.08, 30.04.  $C_{20}H_{23}N_2I$ . Calculated %: I 30.34.

## SUMMARY

Quaternary salts of 2- and 4-phenylacetylenyl- and 2,6-bis(phenylacetylenyl- and 2,6-bis(phenylacetylenyl)-pyridines were prepared. It was shown that these salts are capable of adding sodium hydrosulfide and piperidine and condensing with compounds containing active methyl and methylene groups. They are less reactive than N-methyl-2-phenylacetylenylquinolinium salts. A series of symmetrical and unsymmetrical dyes, mesophenylpyridocarbocyanines, were prepared and their absorption spectra discussed.

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# ORGANOMAGNESIUM SYNTHESIS OF 2-ACETYLENYLQUINOLINIUM SALTS

A. I. Kiprianov and G. G. Dyadyusha

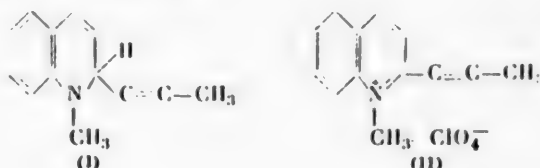
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It is known that by the action of aliphatic and aromatic organomagnesium halides, quaternary salts of quinoline are converted into 1,2-dialkyl- (or 1-alkyl-2-aryl-)1,2-dihydroquinolines, which are readily oxidized by iodine to 2-alkyl-(or 2-aryl-)quinoline alkylidides [1]. The use of acetylenic organomagnesium halides in this reaction offers a new method for the synthesis of quaternary salts with a very reactive triple bond [2, 3]. Only one attempt, and that unsuccessful, to carry out the reaction of quinoline methiodide and an acetylenylmagnesium halide has been described up to now [4].

By the action of propynylmagnesium bromide on quinoline methiodide, we obtained crystalline, unstable 1-methyl-2-propynyl-1,2-dihydroquinoline (I).

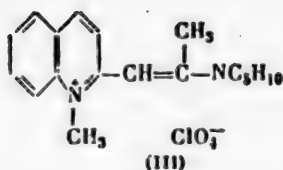


This substance was oxidized by iodine in alcohol, and even with insufficient iodine the difficultly soluble triiodide precipitated. Reduction of the triiodide with sulfur dioxide gave a salt containing two atoms of iodine, probably as a result of the addition of hydrogen iodide at the triple bond. Oxidation of the dihydro derivative with ferric chloride yielded a salt containing iron, but we were unable to obtain it in a pure state. Satisfactory results were obtained by using a saturated solution of ferric sulfate as the oxidant. Treatment of the aqueous alcohol solution formed with perchloric acid precipitated crystalline 1-methyl-2-propynylquinolinium perchlorate (II). The structure of the product was confirmed by the presence of an absorption band at  $2230\text{ cm}^{-1}$  in its infrared spectrum.

For the oxidation by ferric sulfate, it was possible to use the unpurified dihydro derivative and even the ether solution of it obtained after treatment of the organomagnesium synthesis product with ammonium chloride and water. In precisely the same way, from quinoline ethiodide and phenylacetylenylmagnesium bromide we obtained 1-phenylacetylenylquinoline ethoperchlorate, which we had synthesized previously by a different method [2].

The triple bond in 1-methyl-2-propynylquinolinium salts was as reactive in 1-alkyl-2-phenylacetylenylquinolinium salts. The salt (II) readily added piperidine to form the hemicyanine (III).





In the presence of triethylamine the salt (II) condensed in the cold with N-methylrhodanine and also with quaternary salts of quinaldine, 2-methylbenzthiazole, and 2,3,3-trimethylindolenine to yield mesomethylcarbo-cyanines.

The absorption maxima of the dyes synthesized in this way are given in the table and compared with the absorption maxima of the corresponding unsubstituted and mesophenyl-substituted dyes [2, 3].

A comparison of the absorption maxima shows that, despite the difference in electronic nature, like the phenyl group the methyl group in the meso position of unsymmetrical quinocarbocyanines produces a bathochromic displacement of the maximum. This agrees with the treatment of the effect of the substituent in the meso position of symmetrical quinocarbocyanines as a steric effect [5, 7].

No.	Dye formula	Absorption maxima, mμ		
		R=CH <sub>3</sub>	R=C <sub>6</sub> H <sub>5</sub>	R=H
(IV)		649 *	648	607
(V)		596 **	603	582
(VI)		583	596	550
(VII)		580	598; 568	568

\* N,N'-Diethyl derivative,  $\lambda_{\max}$  652.5 mμ [5].

\*\* N,N'-Diethyl derivative, see [6].

#### EXPERIMENTAL

**1-Methyl-2-propynyl-1,2-dihydroquinoline (I).** Allene was passed for 6 hr into 50 ml of an ether solution containing 0.1 mole of ethylmagnesium bromide. Over a period of 1 hr, 25 g of carefully dried and finely ground quinoline methiodide was added with vigorous stirring to the reagent obtained. When all the salt had dissolved, stirring was continued for a further 10 min, and then the reddish, homogeneous mass was poured onto a mixture of 20 g of ammonium chloride and 80 g of ice. The ether layer was separated and the residues washed with 50 ml of ether. The combined ether extracts were washed with water, and the ether was evaporated under reduced

pressure. The dark crystalline mass obtained was recrystallized from 30 ml of methanol. The yield of colorless crystals with m. p. 60-61° was 7.3 g (43%). The substance rapidly darkened and turned to a tar during storage.

Found %: N 7.66, 7.88.  $C_{13}H_{13}N$ . Calculated %: N 7.64.

1-Methyl-2-propynylquinolinium perchlorate (II). A 4.19-g sample of the previous preparation was dissolved in a mixture of 1.25 ml of concentrated sulfuric acid and 20 ml of methanol, and then 25 g of a saturated (40%) aqueous solution of  $Fe_2(SO_4)_3$  and 20 ml of methanol were added. After the mixture had been boiled with activated charcoal and filtered, the filtrate was treated with 4 ml of 40% perchloric acid. A product (3.38 g, 52%) which did not contain iron salts gradually crystallized. It was recrystallized from 80 ml of alcohol. It had m. p. 173°.

Found %: Cl 12.52, 12.57.  $C_{13}H_{12}O_4NCl$ . Calculated %: Cl 12.59.

If the unrecrystallized base was used the yield fell to 42%.

1-Methyl-2-propynylquinolinium triiodide. To a solution of 3.6 g of substance (I) in 40 ml of alcohol was added a solution of 6.08 g of iodine in 60 ml of alcohol. The precipitate formed was collected and washed with alcohol and ether. The brownish leaflets had m. p. 154°; the yield was 5.45 g (44%). After recrystallization from 200 parts of alcohol, the substance had m. p. 156°.

Found %: I 67.96, 67.88.  $C_{13}H_{12}NI_3$ . Calculated %: I 67.63.

1-Ethyl-2-phenylacetylenylquinolinium perchlorate. A mixture of 10 ml of an ether solution containing 0.02 mole of ethylmagnesium bromide and 2.2 ml of phenylacetylene was boiled for 30 min. To the cooled mixture was added 5.7 g of carefully dried and finely ground quinoline ethiodide in 0.5-g portions with vigorous stirring over a period of 40 min. When all the salt had dissolved, stirring was continued for a further 10 min. The mixture was then poured onto a mixture of 3 g of ammonium chloride and 20 g of ice. The ether layer was separated, washed with water, and mixed with a solution of 0.6 ml of sulfuric acid in 10 ml of methanol. To the ether solution were added 10 g of a 40% aqueous solution of  $Fe_2(SO_4)_3$  and 10 ml of methanol. After decolorization by boiling with activated charcoal, the liquid was treated with 2 ml of 40% perchloric acid. A small amount of a dark resin precipitated. After it had been separated, the product began to crystallize slowly. It was recrystallized from 12 parts of methanol. Yellowish tablets with m. p. 160° were obtained in a yield of 1.24 g (17%). The infrared spectrum of a suspension in vaseline oil had absorption bands at 2202 and 2247  $cm^{-1}$ .

Found %: Cl 9.82, 9.86.  $C_{19}H_{16}O_4NCl$ . Calculated %: Cl 9.91.

1-Methyl-2-(2'-piperidylpropenyl)-piperidylpropenylchlorate (III). To a solution of 0.3 g of the perchlorate (II) in 3 ml of methanol was added 0.15 ml of piperidine. A yellow resinous precipitate formed, and this crystallized on standing. It was collected and washed with methanol and ether. We obtained 0.32 g (82%) of the salt with m. p. 159-160° (from 15 parts of methanol). In alcohol,  $\lambda_{max}$  440 m $\mu$  ( $\log \epsilon$  4.32).

Found %: N 7.39, 7.55.  $C_{18}H_{23}O_4N_2Cl$ . Calculated %: N 7.64.

1,1',10-Trimethyl-2,2'-quinocarbocyanine perchlorate (IV, R =  $CH_3$ ). To a solution of 0.5 g of the perchlorate (II) and 0.5 g quinaldine methylmethosulfate in 5 ml of methanol was added 0.25 ml of triethylamine. The dye precipitated as a resin, which crystallized rapidly. The crystals had a green luster and m. p. 179-181° (from methanol) and the yield was 0.52 g (67%). In alcohol  $\lambda_{max}$  649 m $\mu$  ( $\log \epsilon$  4.72).

Found %: N 6.61, 6.65.  $C_{24}H_{23}O_4N_2Cl$ . Calculated %: N 6.38.

1,3',10-Trimethyl-2-quinothiacarbocyanine perchlorate (V, R =  $CH_3$ ). The dye was obtained by the same method from 0.4 g of the perchlorate (II), 0.4 g of 2-methylbenzthiazole methylmethosulfate, and 0.2 ml of triethylamine. The crystals had a green luster and m. p. 212-213° (from methanol), and the yield was 0.48 g (76%). In alcohol  $\lambda_{max}$  596 m $\mu$  ( $\log \epsilon$  4.82).

Found %: N 6.34, 6.33.  $C_{22}H_{21}O_4N_2SCl$ . Calculated %: N 6.30.

1,1',3',3',10-Pentamethyl-2-quinolindocarbocyanine perchlorate (VI, R =  $CH_3$ ). The preparation was obtained in the same way as the previous one from 0.4 g of the perchlorate (II) and 0.45 g of 2,3,3-trimethylindole-nine methiodide. When the product had been recrystallized from methanol, the yield was 0.33 g (51%). The violet tablets had m. p. 178-179°. In alcohol  $\lambda_{max}$  583 m $\mu$  ( $\log \epsilon$  4.52).

Found %: N 6.23, 6.19.  $C_{25}H_{27}O_4N_2Cl$ . Calculated %: N 6.16.

3-Methyl-5-[ $\alpha$ -methyl-8-(1'-methylidihydroquinolylidene-2')-ethylidene]-rhodanine (VII, R=CH<sub>3</sub>). To a mixture of 0.4 g of the perchlorate (II), 0.25 g of N-methylrhodanine, and 5 ml of methanol was added 0.2 ml of triethylamine. The precipitated dye was collected, washed with methanol, and recrystallized from 50 ml of chloroform. The yield was 0.28 g (61%). The dark crystalline powder with a green luster had m. p. 227-228°. In alcohol  $\lambda_{\text{max}}$  580 m $\mu$ .

Found %: S 19.40, 19.20.  $C_{17}H_{16}ON_2S_2$ . Calculated %: S 19.53.

## SUMMARY

A method was developed for preparing 2-acetylenylquinolinium salts from quinoline alkylidides and acetylenic organomagnesium halides. Symmetrical and unsymmetrical carbocyanines with a methyl group in the polymethyne chain were synthesized from 1-methyl-2-propynylquinolinium perchlorate obtained in this way.

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# CHEMISTRY OF DIHYDRORESORCINOL

## VIII. SYNTHESIS BASED ON 2-(3-METHYL-2-BUTENYL)DIHYDRORESORCINOL

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November, 1960

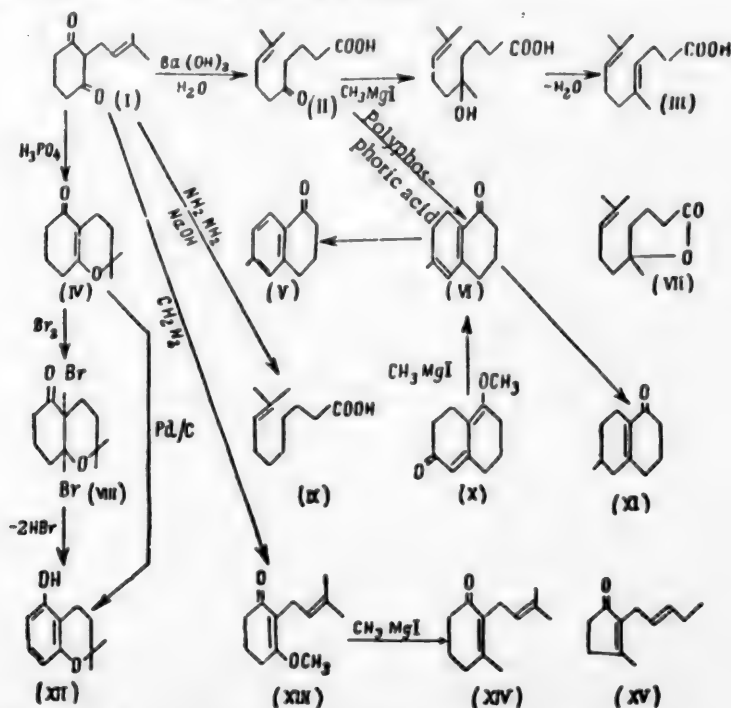
Original article submitted December 10, 1959

Some of the most accessible alkyl derivatives of dihydroresorcinol are derivatives of 2-(3-methyl-2-butenyl)dihydroresorcinol (I), which are readily formed by heating 3-methyl-2-butenyl bromides with the sodium enolate of the  $\beta$ -ketone in methanol [1]. The presence of the allyl double bond in the molecule of 2-(3-methyl-2-butenyl)dihydroresorcinol offers possibilities of using these substances in the synthesis of various aliphatic and cyclic organic compounds.

As the subject of the present investigation we took 2-(3-methyl-2-butenyl)dihydroresorcinol itself, which was described previously by Nazarov et al. [2]. We studied two forms of conversion of this ketone, which proceed with retention and with opening of the cyclohexane nucleus.

When heated with phosphorus pentoxide or phosphoric acid, the diketone (I) underwent cyclization to 2,2-dimethyltetrahydrochroman-5-one (IV) [2], dehydrogenation of which with palladium on charcoal led to 2,2-dimethylchroman-5-ol (XII). The latter could also be obtained by bromination of 2,2-dimethyltetrahydrochroman-5-one and subsequent dehydrobromination of the dibromide (VIII). The structure of 2,2-dimethylchroman-5-ol was confirmed by the fact that its infrared spectrum\* contained characteristic frequencies of a benzene nucleus ( $3000-3100\text{ cm}^{-1}$ ) and a phenolic hydroxyl ( $3420\text{ cm}^{-1}$ ) and also by the formation of the corresponding 3,5-dinitrobenzoate.

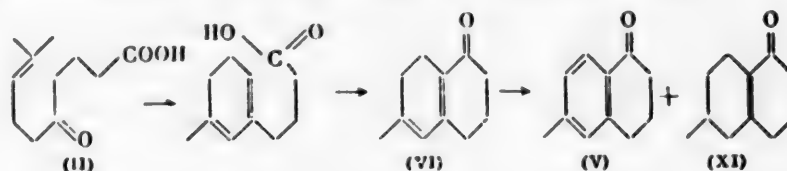
The above conversion represent a new route to the synthesis of chroman derivatives, which form an important class of organic compounds that occur widely in nature.



\* The spectra were plotted by A. F. Vasil'ev on an IKS-12 instrument in chloroform.

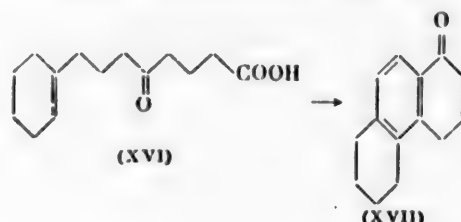
The reaction of the diketone (I) with diazomethane formed the enol ether (XIII), which reacted with methylmagnesium iodide to give 2-(3-methyl-2-butenyl)-3-methyl- $\Delta^8$ -cyclohexan-1-one (XIV). This unsaturated ketone, which is a structural analog of jasmone (XV), had a weak flowerlike odor.

Under the action of boiling barium hydroxide solution, the diketone (I), like other  $\beta$ -carbonyl compounds, underwent hydrolytic cleavage to form 5-keto-9-methyl- $\Delta^8$ -decenoic acid (II). The latter was converted by polyphosphoric acid into  $\epsilon$ -methyl-1-tetralone (V), probably through the intermediate stages of the formation of 1-keto-6-methyl-1,3,7-hexahydronaphthalene (VI) and disproportionation of this:

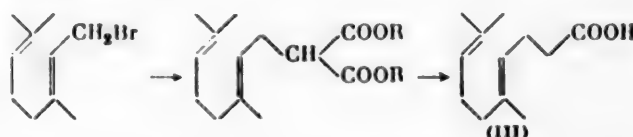


In actual fact, together with 6-methyl-1-tetralone, from the reaction mixture we were able to isolate a ketone (as the 2,4-dinitrophenylhydrazone), which corresponded in elementary analysis and ultraviolet spectrum to 6-methyl- $\Delta^9$ -1-octalone (XI). 6-Methyl-1-tetralone was identical with the bicyclic ketone obtained by the action of methylmagnesium iodide on the methoxy ketone (X) and subsequent aromatization of the dienone (VI).

Thus, 5-keto-9-methyl- $\Delta^8$ -decenoic acid behaves toward polyphosphoric acid like the keto acid (XVI), which is converted into 1-keto-1,3,5,7-octahydrophenanthrene (XVII) under these conditions [3].



The reaction of methylmagnesium iodide with 5-keto-9-methyl- $\Delta^8$ -decenoic acid or, better, with its potassium salt formed geranylacetic acid (III) instead of the expected  $\delta$ -lactone (VII). This conversion, which is a new method of building up isoprenoid chains, may be used in the synthesis of various homologs of geranylacetic acid. According to literature data [4, 5], geranylacetic acid is obtained from geranyl bromide and malonic ester according to the following scheme:



In reductive cleavage by Stetter's method [6], the diketone (I) smoothly gave 9-methyl- $\Delta^8$ -decenoic acid (IX), which was characterized as the S-benzylthiuronium salt.

## EXPERIMENTAL

2,2-Dimethylchroman-5-ol (XII). a) To 12.4 g of 2,2-dimethyltetrahydrochroman-5-one (IV) (b. p. 93-94° at 2 mm [2]) in 70 ml of anhydrous chloroform at about -10° was gradually added 11 g of bromine in 70 ml of anhydrous chloroform and then 120 ml of diethylaniline. After removal of the solvent, the residue was heated at 120-150° for 6 hr. The cooled reaction mixture was dissolved in ether, washed with dilute hydrochloric acid, and carefully extracted with 10% alkali. Acidification of the alkaline solution with hydrochloric acid and subsequent extraction with ether yielded 5.4 g (50%) of compound (XII) with m. p. 119-120° (from heptane).

Found %: C 73.82, 73.80; H 8.01, 7.88.  $C_{11}H_{14}O_2$ . Calculated %: C 74.13; H 7.92.

The 3,5-dinitrobenzoate had m. p. 132-133° (from methanol).

Found %: C 57.81, 57.96; H 4.41, 4.34.  $C_{18}H_{16}O_7N_2$ . Calculated %: C 58.06; H 4.33.

b) A mixture of 1.5 g of 2,2-dimethyltetrahydrochroman-5-one (IV) and 1.3 g of 10% palladium on charcoal was heated at 280-310° for 20 min. The reaction mixture was treated with aqueous alkali and extracted with ether. Treatment of the alkaline solution as described above yielded 0.3 g (20%) of 2,2-dimethylchroman-5-ol (XII) with m. p. 116-118°.

2-(3-Methyl-2-butenyl)-3-methyl- $\Delta^2$ -cyclohexen-1-one (XIV). To an ether solution of diazomethane (from 13.8 g of nitrosomethylurea) was gradually added 12.1 g of 2-(3-methyl-2-butenyl)dihydroresorcinol (m. p. 140°) and the mixture then left at room temperature for 12 hr. We obtained 12 g (92%) of the enol ether (XIII) with b. p. 118-119° (0.05 mm),  $n_D^{20}$  1.5279.

An 11.5-g sample of the enol ether (XIII) was added to a solution of methylmagnesium iodide from 2.9 g of magnesium and 17.2 g of methyl iodide in 500 ml of ether cooled in ice. After it had been stirred at 5° for 6 hr and kept at room temperature for 12 hr, the reaction mixture was treated with dilute hydrochloric acid. From the ether solution we isolated 5.8 g (55%) of 2-(3-methyl-2-butenyl)-3-methyl- $\Delta^2$ -cyclohexen-1-one (XIV) with b. p. 78-80° (0.05 mm),  $n_D^{20}$  1.5092.

Found %: C 81.16, 81.33; H 10.01, 10.20.  $C_{12}H_{18}O$ . Calculated %: C 80.85; H 10.18.

The 2,4-dinitrophenylhydrazone had m. p. 138.5-139.5° (from a mixture of methanol and dioxane) and  $\lambda_{max}$  389 m $\mu$  (alcohol).

Found %: N 16.00, 15.85.  $C_{18}H_{22}O_4N_4$ . Calculated %: N 15.63.

5-Keto-9-methyl- $\Delta^8$ -decenoic acid (II). A mixture of 36 g of the diketone (I) and 100 g of barium hydroxide in 600 ml of water was boiled under reflux for 12 hr. The reaction mixture was cooled and acidified with dilute hydrochloric acid. Extraction with ether gave 30 g (78%) of 5-keto-9-methyl- $\Delta^8$ -decenoic acid (II) with b. p. 155-160° (1 mm) and m. p. 41-42° (from heptane).

Found %: C 66.51, 66.44; H 8.79, 8.78.  $C_{11}H_{18}O_3$ . Calculated %: C 66.64; H 9.15.

6-Methyl-1-tetralone (V). a) A solution of 12.8 g of the methoxy ketone (X) (m. p. 55-56° [7]) in 50 ml of ether was added to the Grignard reagent from 3.8 g of magnesium and 22.5 g of methyl iodide in 100 ml of ether at 0-5°. After the reaction mixture had been kept at room temperature for 5 hr, treatment with dilute hydrochloric acid yielded 7.7 g (66%) of 1-keto-6-methyl-1,3,7-hexahydronaphthalene (VI) with b. p. 87-90° (2 mm),  $n_D^{20}$  1.5505.

The 2,4-dinitrophenylhydrazone had m. p. 223-224° (from a mixture of dioxane and methanol).

Found %: C 59.97, 60.00; H 5.30, 5.34.  $C_{17}H_{16}O_4N_4$ . Calculated %: C 59.64; H 5.30.

A mixture of 3.4 g of 1-keto-6-methyl-1,3,7-hexahydronaphthalene (VI) and 0.67 g of sulfur was heated for 20 min at 180-210°. Vacuum distillation yielded 1.9 g (58%) of 6-methyl-1-tetralone with b. p. 136-138° (9 mm),  $n_D^{20}$  1.5640.

The 2,4-dinitrophenylhydrazone had m. p. 244-245° (from a mixture of methanol and dioxane) and  $\lambda_{max}$  389 m $\mu$  (alcohol).

Found %: N 16.54, 16.64.  $C_{17}H_{16}O_4N_4$ . Calculated %: N 16.46.

The semicarbazone had m. p. 217.5-219.5° (from a mixture of methanol and dioxane).

Found %: C 66.61, 66.60; H 7.17, 7.29.  $C_{12}H_{15}ON_3$ . Calculated %: C 66.74; H 6.96.

6-Methyltetralone obtained by cyclization of  $\gamma$ -(3-methylphenyl)butyric acid had b. p. 129-132° (5 mm) [8].

b) A mixture of 10 g of 5-keto-9-methyl- $\Delta^8$ -decenoic acid (II), 22 g of phosphorus pentoxide, and 22 g of phosphoric acid was heated for 2 hr on a boiling water bath and then treated with a saturated solution of sodium carbonate and extracted with ether. After removal of the solvent, the residue was vacuum distilled. We obtained 4.5 g of a mixture (b. p. 120-137° at 7 mm and  $n_D^{20}$  1.5405-1.5448), which was chromatographed on alumina.



Elution with benzene yielded 1.4 g of a substance with  $n_D^{20}$  1.5430, which was probably 6-methyl- $\Delta^8$ -1-octalone (XI).

The 2,4-dinitrophenylhydrazone had m. p. 222.5-223.5° (from methanol) and  $\lambda_{\max}$  291 m $\mu$  (alcohol).

Found %: C 59.33, 59.92; H 5.38, 5.42.  $C_{17}H_{20}O_4N_4$ . Calculated %: C 59.40; H 5.85.

Subsequent elution with benzene gave 1.7 g (12%) of impure 6-methyl-1-tetralone (V) with b. p. 124-126° (7 mm),  $n_D^{20}$  1.5550.

The 2,4-dinitrophenylhydrazone (m. p. 244.5-245.5°) and the semicarbazone (m. p. 217-219°) did not depress the melting points of the derivatives described above.

Geranylacetic acid (III). a) To a solution of methylmagnesium iodide from 3.3 g of magnesium and 18 g of methyl iodide in 300 ml of ether at -10° was added 10 g of 5-keto-9-methyl- $\Delta^8$ -decenoic acid (II). After being stirred at -10 to 0° for 6 hr and standing at room temperature for 12 hr, the reaction mixture was treated with dilute hydrochloric acid and the ether layer washed with sodium sulfite solution and water. The solvent was removed and the residue vacuum distilled. We obtained 7.7 g (77% of geranylacetic acid (III) with b. p. 119-121° (0.05 mm),  $n_D^{20}$  1.4780.

The S-benzylthiuronium salt had m. p. 118-119° (from aqueous methanol).

Found %: N 7.91, 7.75.  $C_{20}H_{30}O_2N_2S$ . Calculated %: N 7.70.

The salt did not depress the melting point of an authentic sample (m. p. 123.5-125°) prepared by a known method [4].

In the literature [4, 5] it is reported that geranylacetic acid has b. p. 96-97° (0.005 mm),  $n_D^{20}$  1.4740, and the S-benzylthiuronium salt has m. p. 128-129°.

b) To a suspension of the potassium salt of 5-keto-9-methyl- $\Delta^8$ -decenoic acid (II) from 8.2 g of acid in 300 ml of ether at -10° was added an ether solution of methylmagnesium iodide (from 2.52 g of magnesium and 15.7 g of methyl iodide). Treatment as described above yielded 6.5 g (80% of geranylacetic acid (III) with b. p. 129-135° (0.07 mm),  $n_D^{20}$  1.4775.

9-Methyl- $\Delta^8$ -decenoic acid (IX). A 14-g sample of powdered sodium hydroxide was dissolved with heating in 150 ml of diethylene glycol, and then 12.5 g of 2-(3-methyl-2-butenyl)dihydroresorcinol (I), 9 ml of 85% hydrazine hydrate, and a sufficient amount of methanol for the mixture to boil at about 125° were added. The mixture was boiled under reflux for 30 hr and then the boiling point of the mixture raised to 195° by removal of methanol, water, and hydrazine. After the mixture had been heated for 13 hr at this temperature, it was cooled, diluted with water, acidified with hydrochloric acid, and extracted with ether. We obtained 11 g (87%) of 9-methyl- $\Delta^8$ -decenoic acid (IX) with b. p. 146-148° (7 mm),  $n_D^{20}$  1.4555.

Found %: C 71.74; H 11.0.  $C_{11}H_{20}O_2$ . Calculated %: C 71.69; H 10.94.

The S-benzylthiuronium salt had m. p. 140.5-141.5° (from aqueous methanol).

Found %: N 8.60, 8.41.  $C_{19}H_{30}O_2N_2S$ . Calculated %: N 8.00.

#### SUMMARY

1. Bromination and subsequent dehydrobromination of 2,2-dimethyltetrahydrochromanone, which was obtained by cyclization of 2-(3-methyl-2-butenyl)dihydroresorcinol, gave 2,2-dimethylchroman-5-ol, which was also formed by dehydrogenation of 2,2-dimethyltetrahydrochroman-5-one by means of palladium on charcoal.
2. The reaction of the enol ether of 2-(3-methyl-2-butenyl)dihydroresorcinol with methylmagnesium iodide led to 2-(3-methyl-2-butenyl)-3-methyl- $\Delta^2$ -cyclohexen-1-one, which is a structural analog of jasmone.
3. Hydrolytic cleavage of 2-(3-methyl-2-butenyl)dihydroresorcinol yielded 5-keto-9-methyl- $\Delta^8$ -decenoic acid, which was cyclized to 6-methyl-1-tetralone under the action of polyphosphoric acid.
4. The action of methylmagnesium iodide on 5-keto-9-methyl- $\Delta^8$ -decenoic acid or its potassium salt yielded geranylacetic acid.

5. Reductive cleavage of 2-(3-methyl-2-butenyl)dihydroresorcinol by Stetter's method formed 9-methyl- $\Delta^8$ -decenoic acid.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. Some or all of this periodical literature may well be available in English translation. A complete list of the cover-to-cover English translations appears at the back of this issue.

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## SULFONATION AND SULFONIC ACIDS OF ACIDOPHOBIC COMPOUNDS

### XXVIII SULFONATION OF THE COMPOUNDS $R_1R_2C=CH_2$

#### I. GEOMETRIC ISOMERISM OF UNSATURATED SULFONIC ACIDS

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It has been shown [1] that dienes may be sulfonated without appreciable resinification and often in high yields by means of sulfur trioxide bound in a complex with pyridine (pyridine-sulfur trioxide). Styrene is sulfonated readily not only by dioxane-sulfur trioxide [2], but even better by pyridine-sulfur trioxide; however, it is not known which of the geometric isomers of the  $\omega$ -sulfonic acid is thus formed.

To solve this problem we sulfonated hydrocarbons of the type  $R_1R_2C=CH_2$  (styrene,  $\alpha$ -methylstyrene,  $\alpha$ -chlorostyrene, 1,1-diphenylethylene, and  $\alpha$ -vinyl-naphthalene), prepared a series of derivatives of styrene-sulfonic acid and 1,1-diphenylethylene-sulfonic acid, and studied their behavior under irradiation with ultraviolet light. We sulfonated styrene by heating it in a sealed ampoule with twice the molecular amount of pyridine-sulfur trioxide. In the irradiation of  $\omega$ -styrenesulfonic acid derivatives with ultraviolet light it was only in the case of the amide (m. p. 142°) that were able to isolate a second, lower-melting stereoisomer (m. p. 96°). It was evidently the less stable *cis* isomer, as follows in analogy with other unsaturated compounds with stereoisomers. The Raman and infrared spectra of the two forms of  $\omega$ -styrenesulfonamide confirmed that the compounds had different geometric structures [3]. The potassium salt of  $\omega$ -styrenesulfonic acid was also isomerized by irradiation with ultraviolet light, but to a smaller extent than the amide. The sulfonyl chloride obtained from it gave a mixture of the two forms of the amide when treated with ammonium carbonate.

$\alpha$ -Chlorostyrene was sulfonated analogously to styrene. It was found that the reaction formed acetophenonesulfonic acid, which was decomposed to benzoic acid and methanesulfonic acid by heating with barium hydroxide. Acetophenonesulfonic acid synthesized by another method [4] behaved in the same way.

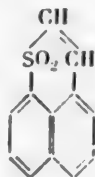
We sulfonated  $\alpha$ -methylstyrene with various sulfonating agents (pyridine-sulfur trioxide, pyridine bis-sulfur trioxide, and dioxane-sulfur trioxide) in various proportions. In all cases we isolated a mixture of mono- and disulfonic acids of  $\alpha$ -methylstyrene, with the unsaturated disulfonic acid predominating.



Experiments on the sulfonation of unsymmetrical diphenylethylene with pyridine-sulfur trioxide did not give positive results.

We obtained the sulfonic acid of 1,1-diphenylethylene only by using pyridine-bis-sulfur trioxide. Diphenylethylene-sulfonic acid should not form geometric isomers. This agrees with our observation that the irradiation of diphenylethylene-sulfonamide with m. p. 133° for 55 hr with ultraviolet light in methanol did not produce a change in the melting point of the amide.

It might have been expected that the sulfonation of  $\alpha$ -vinyl naphthalene with pyridine-sulfur trioxide would form the  $\omega$ -sulfonic acid. However, due to the presence of an active hydrogen in the  $\alpha$ -position of the naphthalene nucleus, an unsaturated cyclic sulfone was formed.



Thus, it was only in the sulfonation of styrene and 1,1-diphenylethylene that we obtained unsaturated monosulfonic acids.

The structure of the sulfonic acids we obtained was demonstrated by oxidation with potassium permanganate in an alkali medium. Benzoic acid was isolated in all cases; sulfo benzoic acid was not detected. Consequently, in sulfonation under mild conditions a sulfonic acid group replaces the hydrogen of the vinyl group and not of the aromatic nucleus (if it is assumed that sulfonation by pyridine-sulfur trioxide proceeds by direct replacement). If sulfonation characterizes the "aromatic" properties of compounds, then it must be considered that the vinyl structure is more "aromatic" than benzene and naphthalene.

## EXPERIMENTAL

### $\omega$ -Styrenesulfonic Acid and Its Derivatives

A mixture of 0.1 mole of styrene, 0.2 mole of pyridine-sulfur trioxide, and 15 ml of dichloroethane was heated in a sealed ampoule at 100-110° for 10 hr. The contents of the ampoule were dissolved in water, treated with concentrated ammonia solution, and washed with dichloroethane to remove pyridine completely. The solution of the ammonium salt was heated with 64 g of barium hydroxide until the smell of ammonia disappeared and the excess barium hydroxide removed with carbon dioxide. The barium salt of styrenesulfonic acid was extracted with hot water and the solution evaporated to dryness on a water bath. The yield of the barium salt was 94%.

Found %: Ba 27.28, 26.90.  $(C_8H_7O_3S)_2Ba$ . Calculated %: Ba 27.27.

The potassium salt of styrenesulfonic acid was obtained from the barium salt by exchange with potassium sulfate.

$\omega$ -Styrenesulfonyl chloride. The contents of the ampoule after the sulfonation of 0.1 mole of styrene were treated with 0.15 mole of phosphorus pentachloride and left at room temperature for 1 hr. The mixture was decomposed with iced water and the styrenesulfonyl chloride washed with water and dried in a desiccator. The yield was 66% and the m. p. 88° (from benzene).

$\omega$ -Styrenesulfonamide.  $\omega$ -Styrenesulfonyl chloride (5 g) was ground carefully with ammonium carbonate and the mixture heated for 1 hr on a water bath and decomposed with water. We obtained 3.2 g of the amide with m. p. 143° (from water).

Found %: N 7.60, 7.90.  $C_8H_7O_2NS$ . Calculated %: N 7.65.

Diethylamide of  $\omega$ -styrenesulfonic acid. To a solution of 5 g of styrenesulfonyl chloride in 50 ml of acetone were added 7.3 g of diethylamine and 2 ml of pyridine. The mixture was left for 30 min and the diethylamide precipitated with water. The yield was 60% and the m. p. 78° (precipitation with water from methanol).

Found %: N 6.22, 6.02.  $C_{12}H_{17}O_2NS$ . Calculated %: N 5.85.

Anilide of  $\omega$ -styrenesulfonic acid. To a solution of 0.01 mole of  $\omega$ -styrenesulfonyl chloride in absolute ether was added 0.02 mole of aniline dropwise and the mixture boiled for 2 hr. The aniline hydrochloride was removed by filtration and the ether evaporated. The residue was dissolved in 5% NaOH and the product precipitated with acid. The anilide of  $\omega$ -styrenesulfonic acid was precipitated with water from methanol and had m. p. 113°.

Found %: N 5.61, 5.67.  $C_{14}H_{13}O_2NS$ . Calculated %: N 5.40.

Ethyl  $\omega$ -styrenesulfonate. To an aqueous solution of 0.008 mole of the barium salt of styrenesulfonic acid was added 0.008 mole of silver sulfate, the mixture evaporated to dryness, and the residue transferred to a round-bottomed flask and boiled in ethyl iodide for 2 hr on a water bath. The excess ethyl iodide was removed by distillation. The ethyl styrenesulfonate was extracted with ether. We obtained 0.5 g of the ester with m. p. 47° (from alcohol).

Found %: C 56.61, 56.76; H 5.75, 5.72; S 15.02, 15.09.  $C_{10}H_{12}O_3S$ . Calculated %: C 56.58; H 5.69; S 15.11.

Methyl  $\omega$ -styrenesulfonate. The contents of the ampoule after sulfonation of 0.025 mole of styrene and 0.04 mole of dimethyl sulfate were heated on a water bath for 8 hr. The cooled reaction mixture was decomposed with 10% ammonia solution and the methyl ester extracted with ether. The yield was 70% and the m. p. 67° (from methanol). The same ester was obtained from the silver salt of  $\omega$ -styrenesulfonic acid and methyl iodide.

Found %: C 54.31; H 5.35.  $C_9H_{10}O_3S$ . Calculated %: C 54.52; H 5.20.

Phenyl  $\omega$ -styrenesulfonate. To a suspension of sodium phenolate in molten phenol (from 0.02 mole of sodium) was added 0.02 mole of styrenesulfonyl chloride and the mixture heated on a water bath and poured into 200 ml of 1 N sodium hydroxide. The phenyl ester was collected and washed with water. The yield was 82% and the m. p. 123° (from alcohol).

Found %: C 64.76, 64.54; H 4.77, 4.66.  $C_{14}H_{12}O_3S$ . Calculated %: C 64.60; H 4.64.

$\omega$ -Styrenesulfonyl fluoride. To a solution of 2 g of  $\omega$ -styrenesulfonyl chloride in xylene was added 6 g of potassium fluoride in 30 ml of water. The emulsion obtained was heated under reflux for 4 hr and the xylene removed by distillation. The substance extracted with ether was a mixture of the acid chloride and the acid fluoride. To separate them the mixture was heated for 2 hr with 10% sulfuric acid, when the acid chloride was hydrolyzed completely. Styrenesulfonyl fluoride was extracted with ether and had m. p. 97° (from methanol).

Found %: F 9.82, 9.97.  $C_8H_7O_2SF$ . Calculated %: F 10.20.

## EXPERIMENTAL

### 1,1-Diphenylethylenesulfonic Acid and Its Derivatives

Into a round-bottomed flask was placed 0.05 mole of pyridine-bis-sulfur trioxide, and 0.05 mole of 1,1-diphenylethylene was added to it dropwise; slight heat evolution was observed. The reaction mixture was heated on a water bath at 70° for 30 min, cooled, decomposed with water, treated with excess barium carbonate, and heated on a water bath until the odor of pyridine disappeared. The barium salt of 1,1-diphenylethylenesulfonic acid was extracted with hot water. The yield was 83%.

Found %: Ba 20.99, 21.27.  $(C_{14}H_{11}O_3S)_2Ba$ . Calculated %: Ba 20.94.

The sodium salt of diphenylethylenesulfonic acid was obtained from the barium salt by exchange with sodium sulfate.

1,1-Diphenylethylenesulfonyl chloride. The product from the sulfonation of 0.025 mole of 1,1-diphenylethylene was heated under reflux with 0.05 mole of phosphorus pentachloride on a water bath for 1 hr. The reaction mixture was decomposed with iced water and the sulfonyl chloride collected by filtration. The yield was 96.5% and the m. p. 65° (decomp.). 1,1-Diphenylethylenesulfonyl chloride was used for further work without additional purification.

1,1-Diphenylethylenesulfonamide. A 2-g sample of diphenylethylenesulfonyl chloride was ground carefully in a mortar with ammonium carbonate and the mixture then heated in a porcelain dish on a water bath. Decomposition of the mixture with water yielded 1.2 g of 1,1-diphenylethylenesulfonamide with m. p. 133-134° (from methanol).

Found %: C 64.67, 64.71; H 5.11, 5.13.  $C_{14}H_{13}O_2NS$ . Calculated %: C 64.84; H 5.05.

The sulfonation of  $\alpha$ -methylstyrene was carried out analogously to the sulfonation of styrene. From 0.1 mole of  $\alpha$ -methylstyrene we isolated 16.6 g of the barium salt.

Found %: Ba 32.11, 31.93.  $(C_9H_9O_3S)_2Ba$ . Calculated %: Ba 25.83.  $C_9H_9O_3S_2Ba$ . Calculated %: Ba 33.21.

Sulfonation of  $\alpha$ -vinyl naphthalene. A mixture of 0.015 mole of  $\alpha$ -vinyl naphthalene, 0.035 mole of pyridine-sulfur trioxide, and 5 ml of dichloroethane was heated in a sealed ampoule at 120-125° for 4 hr. The mixture was decomposed with water and the liberated sulfone collected by filtration. We obtained 1 g of the sulfone with m. p. 218° (from water).

Found %: C 66.59, 66.68; H 4.03, 3.97.  $C_{12}H_9O_2S$ . Calculated %: C 66.63; H 3.72.

#### Irradiation of Sulfonic Acid Derivatives with Ultraviolet Light

PRK-4 and PRK-2 lamps were used as sources of ultraviolet radiation. Solutions in quartz flasks were placed at a distance of 20-25 cm from the lamp. To decrease the evaporation of solvent the irradiation was carried out in flasks with air condensers.

We irradiated  $\omega$ -styrenesulfonamide in benzene and methanol, the diethylamide of styrenesulfonic acid in methanol, diphenylethylenesulfonamide in methanol, the barium and potassium salts of styrenesulfonic acid in water, the anilide and methyl ester of styrenesulfonic acid in methanol, and styrenesulfonyl chloride and fluoride in benzene.

Irradiation of styrenesulfonamide. A solution of 2 g of the amide with m. p. 143° in methanol was irradiated with ultraviolet light for 100 hr. The solution had a dark red color after irradiation. The methanol was removed by distillation, and the residual tarry material crystallized after some time. After recrystallization from water, the amide had m. p. 94-95°, after a second recrystallization from water, it had m. p. 96°, and after recrystallization from alcohol, it had m. p. 96°. The amide was isomerized completely, but approximately 50% was converted into resin.

Found %: N 7.80, 7.83.  $C_8H_9O_2NS$ . Calculated %: N 7.65.

1,1-Diphenylethylenesulfonamide with m. p. 134° (0.8 g) in methanol was irradiated for 65 hr; we isolated an amide with m. p. 131°. A mixed melting point with unirradiated 1,1-diphenylethylenesulfonamide was not depressed.

#### SUMMARY

Styrene,  $\alpha$ -chlorostyrene,  $\alpha$ -methylstyrene, 1,1-diphenylethylene, and  $\alpha$ -vinyl naphthalene were sulfonated with pyridine-sulfur trioxide; a series of derivatives of  $\omega$ -styrenesulfonic acid and 1,1-diphenylethylenesulfonic acid were obtained.

It was found that  $\omega$ -styrenesulfonamide was converted into a geometric isomer by the action of ultraviolet light. 1,1-Diphenylethylene-2-sulfonamide was not changed by the action of ultraviolet light.

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# SYNTHESIS OF FURAN, PYRROLE, NAPHTHOFURAN, AND BENZINDOLE DERIVATIVES

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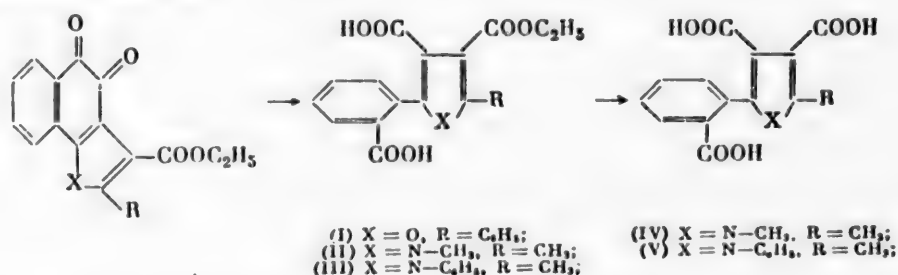
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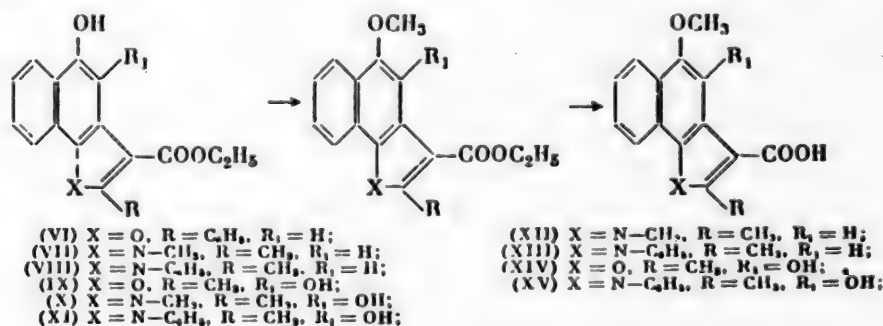
November, 1960

Original article submitted December 7, 1959

In some of our previous work [1] 5-hydroxynaphthofurans and 5-hydroxybenzindoles were oxidized to o-quinones with chromic acid. The oxidation of the latter with hydrogen peroxide in alkaline solution yielded derivatives of furan and pyrrole (I)-(III). Hydrolysis of the pyrrole derivatives (II) and (III) led to tribasic acids of the pyrrole series (IV) and (V).



In addition, in order to synthesize substance with a potential plant-growth-stimulating action, we methylated derivatives of 5-hydroxy- and 4,5-dihydroxynaphthofuran and benzindole which were obtained previously [1-4]. The action of excess dimethyl sulfate on 4,5-dihydroxynaphthofurans and 4,5-dihydroxybenzindoles resulted in the methylation of only one hydroxyl group, probably in position 5. In contrast to derivatives of 5-hydroxynaphthofuran and 5-hydroxybenzindole, the monomethoxy derivatives obtained reacted with ferric chloride and copper acetate.



## EXPERIMENTAL

1,1-Dimethyl-3-carbethoxy-4-carboxy-5-(2'-carboxyphenyl)-pyrrole (II). With vigorous stirring at room temperature, 15.5 ml of 30% hydrogen peroxide and 22 ml of 2 N sodium hydroxide were added over a period

TABLE 1

## Furan and Pyrrole Derivatives

starting material		Reagents			Compound obtained	Melting point (from methanol)	Empirical formula	% C		% H		Yield (g)
		amt. (g)	NaOH	30% H <sub>2</sub> O <sub>2</sub> (ml)	solvent (ml)			found	calcd.	found	calcd.	
2-Phenyl-3-carbethoxy-4,5-dioxonaphthofuran		1.72	10 ml, 2 N soln.	6.25	Methanol 80	210—211°	C <sub>21</sub> H <sub>16</sub> O <sub>7</sub>	66.08, 66.18	66.31	4.30, 4.33	4.24	0.9
1,2-Dimethyl-3-carbethoxy-4,5-dioxobenzindole		3	22 ml, 2 N soln.	15.5	Methanol 125	183—184 (decomp.)	C <sub>17</sub> H <sub>17</sub> O <sub>6</sub> N	61.66, 61.52	61.63	5.27, 5.26	5.17	2.21
1-Phenyl-2-methyl-3-carbethoxy-4,5-dioxobenzindole		2.88	20 ml, 2 N soln.	12	Methanol 150	193—195	C <sub>22</sub> H <sub>18</sub> O <sub>6</sub> N	67.42, 67.28	67.17	4.92, 5.17	4.87	2.53
1,2-Dimethyl-3-carbethoxy-4-carboxy-5-(2'-carboxyphenyl)-pyrrole (II)		1.38	1.6 g, solid	—	Ethanol 40	207—209	C <sub>15</sub> H <sub>13</sub> O <sub>6</sub> N	59.43, 59.51	59.40	4.36, 4.43	4.32	1.19
1-Phenyl-2-methyl-3-carbethoxy-4-carboxy-5-(2'-carboxyphenyl)-pyrrole (III)		1.93	2.0 g, solid	—	Ethanol 45	230—232	C <sub>20</sub> H <sub>15</sub> O <sub>6</sub> N	65.35, 65.40	65.75	4.16, 4.23	4.14	1.75

TABLE 2

## Methylation of Naphthofuran and Benzindole Derivatives

Reagents				Methoxy derivative obtained	M.P. (re-crystalliza- tion solvent)	Empirical formula	% G		% H		Yield (g)	
starting material		dimethyl sulfate (ml)	2 N NaOH (ml)				dioxane (ml)	found	calcd.	found		calcd.
name	amt. (g)											
2-Phenyl-3-carbethoxy-5- hydroxynaphthofuran	4.48	5	25	10	112.5° (from alco- hol)	$C_{22}H_{18}O_4$	76.40, 76.61	76.28	5.35, 5.27	5.24	4.7	
1,2-Dimethyl-3-carbethoxy- 5-hydroxybenzindole	4.25	5	25	10	228—229 (from acetic acid)	$C_{13}H_{19}O_3N$	72.45, 72.34	72.70	6.09 6.19	6.44	4.4	
1-Phenyl-2-methyl-3-car- bethoxy-5-hydroxy- benzindole	5.18	5	25	10	120—122 (from alco- hol)	$C_{23}H_{21}O_3N$	76.81, 76.61	76.86	5.85, 5.85	5.89	5.32	
2-Methyl-3-carbethoxy- 4,5-dihydroxynaphthofuran	1.3	3.3	16.5	7	126—126.5 (from alco- hol)	$C_{17}H_{16}O_5$	67.50, 67.73	67.99	5.35, 5.34	5.37	0.6	
1,2-Dimethyl-3-carbethoxy- 4,5-dihydroxybenzindole	6.3	15	76	30	210 (from dioxane)	$C_{18}H_{18}O_4N$	63.63, 63.79	63.99	6.20, 6.18	6.11	4.32	
1-Phenyl-2-methyl-3-car- bethoxy-4,5-dihydroxy- benzindole	3.85	7	35	15	186—187.5 (from alco- hol)	$C_{23}H_{21}O_4N$	73.16, 73.18	73.58	5.74, 5.82	5.64	3.44	

TABLE 3

## Hydrolysis of Naphthofuran and Benzindole Derivatives

Reagents		Compound obtained	Melting point (re-crystallization solvent)	Empirical formula	% C		% H		Yield (g)		
starting material name	amount (g)				alcohol (ml)	NaOH (g)	found	calcd.		found	calcd.
1,2-Dimethyl-3-carb-ethoxy-5-methoxybenzindole (VII)	4.82	50	3.4	1,2-Dimethyl-3-carboxy-5-methoxybenzindole (XII)	231—232 <sup>a</sup> (from acetic acid)	C <sub>16</sub> H <sub>15</sub> O <sub>3</sub> N	71.43, 71.36	71.36	5.94, 6.01	5.61	2.93
1-Phenyl-2-methyl-3-carb-ethoxy-5-methoxybenzindole (VIII)	2.85	25	1.5	1-Phenyl-2-methyl-3-carboxy-5-methoxybenzindole (XIII)	201—202 (from di-oxane)	C <sub>21</sub> H <sub>17</sub> O <sub>3</sub> N	76.29	76.12	5.38	5.17	1.59
2-Methyl-3-carb-ethoxy-4-hydroxy-5-methoxynaphthofuran (IX)	0.7	12	0.5	2-Methyl-3-carboxy-4-hydroxy-5-methoxynaphthofuran (XIV)	210—212 (from di-oxane)	C <sub>13</sub> H <sub>12</sub> O <sub>5</sub>	65.91	66.17	4.49	4.44	0.4
1-Phenyl-2-methyl-3-carb-ethoxy-4-hydroxy-5-methoxybenzindole (XI)	1.74	15	1.0	1-Phenyl-2-methyl-3-carboxy-4-hydroxy-5-methoxybenzindole (XV)	223—224 (from di-oxane)	C <sub>21</sub> H <sub>17</sub> O <sub>4</sub> N	72.31, 72.25	72.61	5.25, 5.28	4.93	1.0

of approximately 5 min to a suspension of 3 g of 1,2-dimethyl-3-carbethoxy-4,5-dioxobenzindole in 125 ml of methanol. The solution temperature thereupon rose by 10° and the solution became lighter. The solution was then stirred for 30 min, diluted with 3-5 volumes of water, and filtered. The filtrate was acidified to Congo with concentrated hydrochloric acid. The crystals of the pyrrole derivative (II) liberated were dried and recrystallized from methanol. The yield was 2.21 g and the m. p. 183-184° (decomp.).

Found %: C 61.66, 61.52; H 5.27, 5.26.  
 $C_{17}H_{17}O_6N$ . Calculated %: C 61.63; H 5.17.

The other o-quinones were oxidized with hydrogen peroxide analogously (Table 1).

1,2-Dimethyl-3,4-dicarboxy-5-(2'-carboxy-phenyl)-pyrrole (IV). A 1.38-g sample of the pyrrole derivative (II) was dissolved in a solution of 1.6 g of sodium hydroxide in 40 ml of alcohol. The reaction solution was boiled on a water bath for 1 hr, then diluted with two volumes of water, and boiled for 30 min. The solution obtained was filtered and acidified to Congo with concentrated hydrochloric acid. The precipitate was collected and dried. The yield was 1.19 g and the m. p. 207-209° (from methanol).

Found %: C 59.43, 59.51; H 4.36, 4.43.  
 $C_{15}H_{13}O_6N$ . Calculated %: C 59.40; H 4.32.

The other pyrrole derivative (III) was hydrolyzed analogously (Table 1).

2-Phenyl-3-carbethoxy-5-methoxynaphthofuran (VI). A 4.48-g sample of the 5-hydroxynaphthofuran derivative was dissolved in 10 ml of dioxane. To the solution obtained were added 25 ml of 2 N sodium hydroxide and 5 ml of dimethyl sulfate. The reaction solution was shaken in a closed vessel at room temperature for 45 min, treated with three volumes of water, and cooled. The crystals liberated were collected. The yield was 4.7 g and the m. p. 112.5° (from alcohol).

Found %: C 76.40, 76.61; H 5.35, 5.27.  
 $C_{22}H_{18}O_4$ . Calculated %: C 76.28; H 5.24.

The other 5-methoxy derivatives of naphthofuran and benzindole (VII-XI) were synthesized analogously (Table 2). Some of the derivatives of benzofuran and benzindole obtained [(VII), (VIII), (IX), and (XI)] were hydrolyzed to the corresponding naphthofuran- and benzindolecarboxylic acids (XII)-(XV) under the conditions of the previous experiments (Table 3).

### SUMMARY

It was shown that o-quinones of the naphthofuran and benzindole series are converted to furan and pyrrole derivatives by hydrogen peroxide in an alkaline solution.

Derivatives of 5-methoxynaphthofuran and 5-methoxybenzindole were synthesized for testing as plant-growth stimulants.

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# CHEMISTRY OF SELENOPHENE

## XXXI. REACTIONS OF 5-NITROSELENOPHENE-2-CARBONYL CHLORIDE AND 5-NITRO-2-DIAZOACETOSELENOPHENE

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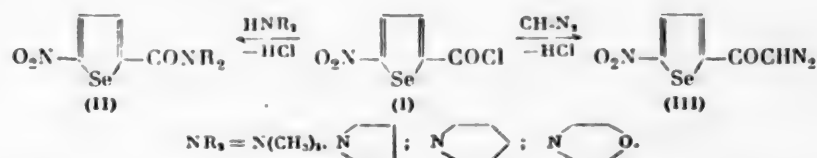
November, 1960

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In the present work 5-nitroselenophene-2-carbonyl chloride (I), from which we previously prepared 5-nitro-2-acetoselenophene [1], was used for the synthesis of a series of substituted amides of 5-nitroselenophene-2-carboxylic acid (II) and also  $\omega$ -derivatives of 5-nitro-2-acetoselenophene.

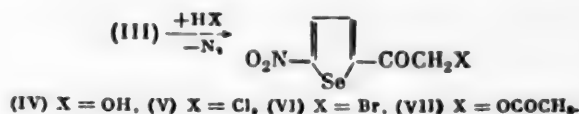
By the reaction of this acid chloride with dimethylamine, pyrrolidine, piperidine, and morpholine, we prepared the dimethylamide of 5-nitroselenophene-2-carboxylic acid, 1-(5'-nitroselenenoyl-2)-morpholine.

We also treated 5-nitroselenophene-2-carbonyl chloride with diazomethane and obtained 5-nitro-2-diazoacetoselenophene (III) in 70.5% yield.



The ether solution of diazomethane (obtained from nitrosomethylurea [2]) required preliminary distillation, as traces of alkali produced tar formation and the yield of 5-nitro-2-diazoacetoselenophene fell sharply. It should be noted that by application of this method in the nitrofuran series, the reaction of the acid chloride of the appropriate acid and diazomethane [3] yielded 5-nitro-2-diazoacetofuran in 83.5% yield, while this reaction has not been investigated as yet in the thiophene series.

By hydrolysis of 5-nitro-2-diazoacetoselenophene with dilute sulfuric acid we obtained a good yield (96%) of 5-nitro-2-hydroxyacetoselenophene (IV). The action of hydrogen chloride or bromide on the diazo ketone formed 5-nitro-2-chloroacetoselenophene (V) (92.5%) and 5-nitro-2-bromoacetoselenophene (VI) (84%), while the action of acetic acid yielded 5-nitro-2-acetoxyacetoselenophene (VII) (88.5%). We also prepared the latter by acylating 5-nitro-2-hydroxyacetoselenophene with acetyl chloride but in low yield (14.5%) due to tar formation.



5-Nitro-2-chloroacetofuran (96%) and 5-nitro-2-bromoacetofuran (85.5%) were prepared analogously in the nitrofuran series [4].



## EXPERIMENTAL

5-Nitroselenophene-2-carboxyl chloride (I). A mixture of 1.1 g of 5-nitroselenophene-2-carboxylic acid and 4.1 g of thionyl chloride was boiled for 1.5 hr and then the excess thionyl chloride removed in vacuum at 50°. Benzene (7 ml) was added and removed in vacuum at 50° and this operation repeated twice for the complete removal of thionyl chloride. We obtained 0.95 g (80%) of yellow crystals with m. p. 43-45°. This preparation of the acid chloride could be used successfully for subsequent syntheses without further purification; a pure product melts at 53-53.5° [1].

1-(5'-Nitroselenenoyl-2')-pyrrolidine. A solution of 0.37 g of pyrrolidine in 1 ml of benzene was added dropwise with stirring and cooling in ice and salt to the acid chloride (I) (from 0.58 g of acid and 2.15 g of thionyl chloride) in 3.5 ml of benzene and the mixture left at 20° for 2 hr. To the mixture was added 30 ml of chloroform and the solution washed with water and dried with anhydrous sodium sulfate. After removal of the solvents, the residue was recrystallized from 50% alcohol. We obtained 0.55 g (76.5%, calculated on the acid, and 95.5%, calculated on the acid chloride) of yellow crystals with m. p. 164-165°.

Found %: C 39.80, 39.68; H 3.83, 3.81; Se 28.70, 28.68.  $C_9H_{10}O_3N_2Se$ . Calculated %: C 39.57; H 3.69; Se 28.91.

1-(5'-Nitroselenenoyl-2')-piperidine. As described above, the reaction of the acid chloride (I) (from 0.58 g of acid and 2.15 g of thionyl chloride) and 0.44 g of piperidine yielded 0.6 g (72.5%, calculated on the acid, and 99%, calculated on the acid chloride) of yellow crystals with m. p. 73.5-74° (from 50% alcohol).

Found %: C 41.53, 41.54; H 4.54, 4.38; Se 27.18, 27.24.  $C_{10}H_{12}O_3N_2Se$ . Calculated %: C 41.82; H 4.21; Se 27.46.

N-(5-Nitroselenenoyl-2)-morpholine. As described above, the reaction of the acid chloride (I) (from 0.58 g of acid and 2.15 g of thionyl chloride) and 0.46 g of morpholine yielded 0.62 g (81.5%, calculated on the acid, and ~100% calculated on the acid chloride) of yellow crystals with m. p. 101-102° (from 50% alcohol).

Found %: C 37.21, 37.29; H 3.57, 3.57; Se 27.00, 27.14.  $C_9H_{10}O_4N_2Se$ . Calculated %: C 37.38; H 3.48; Se 27.31.

Dimethylamide of 5-nitroselenophene-2-carboxylic acid. With stirring and cooling, a mixture of 1.13 g of dimethylamine hydrochloride and 0.46 g sodium hydroxide in 1.5 ml of water was added dropwise to the acid chloride (I) (from 0.58 g of acid and 2.15 g of thionyl chloride) in 2.5 ml of acetone. The precipitate was collected and washed with water. We obtained 0.41 g (63%, calculated on the acid, and 79%, calculated on the acid chloride) of light yellow needles with m. p. 105-106° (from water).

Found %: C 34.18, 34.38; H 3.52, 3.45; Se 31.87, 31.84.  $C_7H_8O_3N_2Se$ . Calculated %: C 34.02; H 3.26; Se 31.95.

5-Nitro-2-diazoacetoselenophene (III). A solution of the acid chloride (I) (from 11.8 g of acid and 41 g of thionyl chloride) in 80 ml of absolute ether was added dropwise at 0° to a distilled ether solution of diazomethane (100 ml) (from 30 g of nitrosomethylurea [2]); there was vigorous evolution of nitrogen bubbles. The flask with a calcium chloride tube was left in the dark at 0° for 2 hr and then at 20° for 16 hr. The precipitate was collected and washed with ether. We obtained 5.19 g of the diazo ketone. Evaporation of the filtrate to 20 ml at a temperature of no higher than 30° yielded a further 2.18 g of less pure diazo ketone. The yield was 7.37 g (56.5%, calculated on 5-nitroselenophene-2-carboxylic acid, and 70.5%, calculated on the acid chloride) and the m. p. 118-119° (decomp., from 50% alcohol); the product formed yellow crystals.

Found %: C 29.62, 29.81; H 1.46, 1.57; Se 32.15, 32.25.  $C_6H_3O_3N_3Se$ . Calculated %: C 29.52; H 1.24; Se 32.35.

When an unredistilled ether solution of diazomethane was used, the yield of the diazo ketone did not exceed 33% [calculated on the acid chloride (I)].

5-Nitro-2-hydroxyacetoselenophene (IV). A mixture of 3.2 g of 5-nitro-2-diazoacetoselenophene and 40 ml of 4% sulfuric acid was heated on a boiling water bath for 30 min until the evolution of nitrogen ceased, and then cooled with ice. We obtained 2.95 g (96%) of yellow crystals with m. p. 108-109° (from water).

Found %: C 31.13, 31.21; H 2.40, 2.37; Se 33.52, 33.64.  $C_6H_5O_4NSe$ . Calculated %: C 30.79; H 2.15; Se 33.72.

Semicarbazone. From 0.58 g of the ketone (IV), 0.28 g of semicarbazide hydrochloride, and 0.45 g of sodium acetate in 50 ml of water we obtained 0.64 g (88.5%) of yellow crystals with m. p. 227-229° (decomp., from alcohol).

Found %: C 29.13, 28.79; H 2.96, 3.06; Se 26.92, 26.98.  $C_7H_5O_4N_2Se$ . Calculated %: C 28.88; H 2.77; Se 27.12.

5-Nitro-2-chloroacetoselenophene (V). A 0.7-g sample of 5-nitro-2-diazoacetoselenophene was added to 30 ml of absolute ether saturated with dry hydrogen chloride and the mixture left at 20° for 4 hr. Evaporation of the ether yielded 0.67 g (92.5%) of the chloro ketone with m. p. 131-131.5° (from ligroin); the product formed yellow needles.

Found %: C 28.17, 28.18; H 1.81, 1.56; Se 28.58, 28.67.  $C_6H_4O_3NClSe$ . Calculated %: C 28.53; H 1.60; Se 28.89.

5-Nitro-2-bromoacetoselenophene (VI). With cooling in ice and shaking, 1.5 ml of 41% hydrobromic acid was added to 0.61 g of 5-nitro-2-diazoacetoselenophene in 50 ml of ether, stirring continued for a further hour, and the mixture extracted with ether. The ether extracts were washed with water and dried with anhydrous sodium sulfate, and the ether was evaporated. We obtained 0.62 g (84%) of the bromo ketone with m. p. 125.5-126° (from ligroin); the product formed yellow crystals.

A mixed melting point with a preparation of 5-nitro-2-bromoacetoselenophene [5] obtained by bromination of 5-nitro-2-acetoselenophene was not depressed.

5-Nitro-2-acetoxyacetoselenophene (VII). a) A mixture of 0.7 g of 5-nitro-2-diazoacetoselenophene and 4.5 ml of glacial acetic acid was boiled for 40 min, cooled, diluted with 10 ml of water, and neutralized with sodium bicarbonate and the precipitate collected. We obtained 0.7 g (88.5%) of the acetate as yellow crystals with m. p. 97.5-98° (from ligroin).

Found %: C 34.73, 34.80; H 2.71, 2.68; Se 28.29, 28.38.  $C_6H_7O_5NSe$ . Calculated %: C 34.79; H 2.55; Se 28.59.

b) To a stirred solution of 0.58 g of 5-nitro-2-hydroxyacetoselenophene in 3 ml of glacial acetic acid was added 1.5 ml of acetyl chloride dropwise. The mixture was heated at 50° for 30 min, cooled, and poured into 50 ml of water and the precipitate collected. We obtained 0.1 g (14.5%) of the acetate with m. p. 97.5-98° (from ligroin). A mixed melting point with the previous preparation of (VII) was not depressed.

#### SUMMARY

1. The reaction of 5-nitroselenophene-2-carbonyl chloride with secondary amines proceeds smoothly and leads to the corresponding substituted amides of this acid.

2. 5-Nitroselenophene-2-carbonyl chloride reacts readily with diazomethane to form 5-nitro-2-diazoacetoselenophene, hydrolysis of which leads to 5-nitro-2-hydroxyacetoselenophene, and chlorolysis and bromolysis of the latter give 5-nitro-2-chloroacetoselenophene and 5-nitro-2-bromoacetoselenophene, respectively, while acetolysis gives 5-nitro-2-acetoxyacetoselenophene.

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## INVESTIGATION OF ISOXAZOLES

### XI. CONDENSATION OF ISOXAZOLES WITH AROMATIC ALDEHYDES

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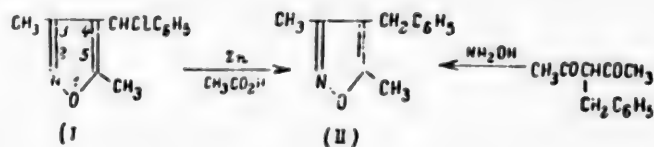
November, 1960

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The analogy in the properties of the isoxazole and pyridine nuclei, which was pointed out previously on the basis of an investigation of electrophilic substitution of some isoxazole derivatives, carried out in our laboratory [1, 2], makes it interesting to study other reactions for comparing the behavior of the two heterocyclic systems. One characteristic of pyridine derivatives is the capacity of the methyl groups in  $\alpha$ - and  $\gamma$ -picolines for crotonic condensation with aldehydes [3]. Reactions of this type, which are also characteristic of some other aromatic heterocyclic systems (thiazole and oxazole), have hardly been studied for isoxazole derivatives. The only examples of this type of reaction are crotonic condensation of 3,5-dimethyl- and 3-phenyl-5-methyl-4-nitroisoxazoles [4] and also quaternary salts of 3-methyl-5-phenyl- and 3,5-dimethylisoxazole [5]. However, due to the well-known activation of the methyl group by a nitro group and a quaternary ammonium grouping, these reactions do not characterize the effect of the heterocyclic nucleus of isoxazole itself on the lability of the hydrogen atoms of the methyl groups.

In order to determine the capacity of methyl groups attached to an unactivated isoxazole nucleus for crotonic condensation, we studied the condensation of some methylisoxazoles with aromatic aldehydes. The reaction was studied mainly on the interaction of 3,5-dimethylisoxazole and benzaldehyde. A condensation in the presence of acetic anhydride or zinc chloride under conditions typical of the condensation of picolines with aldehydes gave negative results due to strong tar formation; no substances containing an isoxazole nucleus could be isolated. Condensation did not occur in the presence of diethylamine.

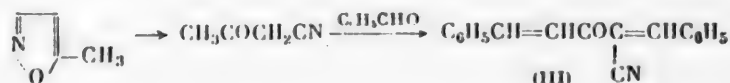
A positive result was obtained by heating a mixture of 3,5-dimethylisoxazole and benzaldehyde in the presence of dry hydrogen chloride in a sealed ampoule at 90-100°. However, the substance with the composition  $C_{12}H_{12}ONCl$  obtained in this way did not correspond in its properties to the condensation product of dimethylisoxazole through one of the methyl groups; in particular, it was impossible to prepare the corresponding styryl derivative from it. In actual fact, the substance obtained was found to be phenyl-(3,5-dimethylisoxazolyl-4)-chloromethane (I), i.e., it was formed as a result of condensation at position 4 of the isoxazole nucleus. The structure of this substance was demonstrated by reducing it with zinc in acetic acid [6] to 3,5-dimethyl-4-benzylisoxazole [2], which was identical with the substance obtained by synthesis from  $\alpha$ -benzylacetylacetone.



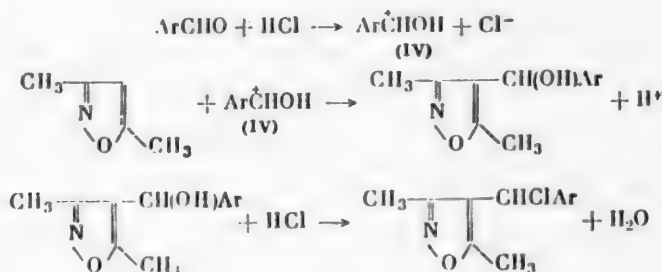
The yield of the condensation product of 3,5-dimethylisoxazole and benzaldehyde depended strongly on the reaction conditions. The best results were obtained by heating an equimolecular mixture of the components in the presence of 0.7-0.8 equiv. of hydrogen chloride for 35 hr.

We attempted to extend the reaction to other aldehydes and isoxazole derivatives. Of the aldehydes, only *p*-tolualdehyde and cumaldehyde gave condensation products, but in yields of 18 and 14% on the 3,5-dimethylisoxazole introduced into the reaction. Condensation products could not be obtained with anisaldehyde,  $\alpha$ -naphaldehyde, *m*-nitrobenzaldehyde, 2,4-dinitrobenzaldehyde, or chloral.

An attempt to carry out the reaction with monomethylisoxazoles did not give positive results, as the latter were found to be insufficiently stable under the reaction conditions. From the products of the reaction of 5-methylisoxazole and benzaldehyde we were able to isolate a crystalline substance, which could be assigned the structure of  $\alpha$ -cyanodibenzalacetone (III) on the basis of analysis data; its formation may be explained by initial opening of the 5-methylisoxazole ring [7] and subsequent condensation of the  $\beta$ -keto-butyronitrile formed with benzaldehyde.



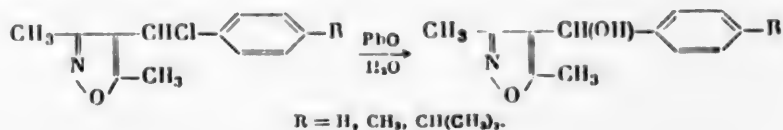
The formation of substituted aryl-(3,5-dimethylisoxazolyl-4)-chloromethanes by condensation of 3,5-dimethylisoxazole with aromatic aldehydes is the result of a reaction which is similar in character to the chloromethylation of isoxazoles that was studied in our laboratory [2], though it requires considerably more drastic conditions. The mechanism of this reaction can evidently be illustrated by a scheme analogous to that adopted for chloromethylation.



This mechanism is compatible with the need to use more drastic conditions in the given reaction than in chloromethylation. It is clear that the electrophilic activity of the carbonium cation (IV) is low in our case due to the nucleophilicity of the neighboring aromatic nucleus.

Thus, while picoline reacts through its methyl group in condensation with aldehydes, on the contrary, the nucleus reacts in dimethylisoxazole. This sharp difference in the behavior of these two heterocyclic systems is the logical consequence of the considerably higher tendency of the isoxazole nucleus for electrophilic substitution in comparison with the pyridine nucleus and considerably less manifestation of the free electron pair at the nitrogen atom in the ring.

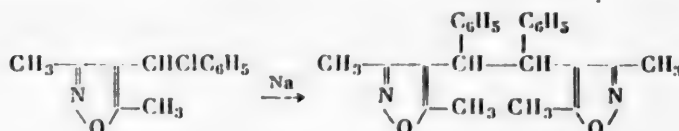
The halogen derivatives of isoxazole obtained by the procedure described in this communication are analogous to benzohydril chloride, and the halogen atom should be quite labile, a fact which may be used in the synthetic chemistry of isoxazole. Thus, treatment of a suspension of them in boiling water with freshly precipitated lead oxide, as we described [2] for the hydrolysis of chloromethylation products, gave a high yield of isoxazolylaryl-carbinols, analogous to benzohydrol.



The carbinols obtained could then be oxidized with chromic anhydride to ketones, analogously to benzophenone, which could also be prepared by direct oxidation of the chlorides with chromic mixture.

In the oxidation of *p*-tolyl-(3,5-dimethylisoxazolyl-4)-chloromethane with chromic mixture, together with oxidation of the chloromethyl group to a carbonyl group, there was oxidation of the methyl group in the aromatic nucleus, and 3,5-dimethyl-4-(*p*-carboxybenzoyl)-isoxazole was formed. As is known [2], methyl groups of the isoxazole ring are resistant to oxidation under these conditions.

Finally, we made an attempt to prepare the isoxazole analog of the known antihistaminic preparation dimedrol (O-benzohydril ether of  $\beta$ -dimethylaminoethanol) by condensation of phenyl-(3,5-dimethylisoxazolyl-4)-chloromethane with dimethylaminoethanol in the presence of sodium. However, the only compound which could be isolated from the reaction was the product of a Wurtz condensation, namely 1,2-diphenyl-1,2-di-(3',5'-dimethylisoxazolyl-4')-ethane.



## EXPERIMENTAL

**Aryl-(3,5-dimethylisoxazolyl-4)-chloromethanes.** An equimolecular mixture of 3,5-dimethylisoxazole and freshly distilled aromatic aldehyde with 0.75-0.77 equiv. of dry hydrogen chloride was heated in a sealed ampoule on a boiling water bath for 35 hr. The reaction mixture was then poured into an equal volume of water, neutralized with sodium carbonate, and extracted with benzene. The benzene extracts were dried over calcium chloride, the solvent and unreacted starting materials removed by distillation in a stream of nitrogen and the residue vacuum distilled.

The substance obtained was contaminated with a small amount of aldehyde, and for removal of this the substance was left for several days in air; during this time the aldehyde was oxidized to the acid, which was removed by extraction with potassium carbonate solution; the substance was extracted with benzene, the extracts were dried over calcium chloride, and after removal of the solvent, the residue was vacuum distilled (Table 1).

The aryl-(3,5-dimethylisoxazolyl-4)-chloromethanes obtained were odorless yellowish oils, which were readily soluble in organic solvents and stable during storage.

**Condensation of 5-methylisoxazole with benzaldehyde.** The reaction was carried out as above with 8.3 g of 5-methylisoxazole, 10.6 g of benzaldehyde, and 1.5 g of hydrogen chloride. After treatment of the reaction mixture with water, the precipitate was collected and washed with ether on the filter. We obtained 1.5 g of  $\alpha$ -cyanodibenzalacetone with m. p. 144-147°. After three recrystallizations from benzene, the substance had m. p. 152.5°.

The fine lemon crystals were readily soluble in chloroform and dichloroethane, sparingly soluble in ether, acetone, and ligroin, and insoluble in water. A solution in chloroform decolorized bromine water and permanganate solution.

Found %: C 83.16, 83.00; H 5.13, 5.12; N 5.15, 5.01.  $C_{18}H_{15}ON$ . Calculated %: C 83.38; H 5.05; N 5.40.

**Aryl-(3,5-dimethylisoxazolyl-4)-carbinols.** A solution of the aryl-(3,5-dimethylisoxazolyl-4)-chloromethane in dioxane was added dropwise with stirring to a suspension of a 2-fold excess of freshly precipitated lead oxide in boiling water; the reaction mixture was then boiled with stirring for 15 min and cooled and the precipitate removed and washed with chloroform on the filter. The filtrate was extracted with chloroform and the combined extracts were dried over magnesium sulfate. After removal of the solvent, the residue was vacuum distilled. The yields, constants, and analyses of the carbinols obtained are given in Table 2.

The substances obtained were yellowish, odorless, very viscous oils,\* which were readily soluble in chloroform, ether, and benzene and sparingly soluble in methanol and ligroin. They were stable during storage.

\* On prolonged standing phenyl-(3,5-dimethylisoxazolyl-4)-carbinol formed fine colorless crystals with m. p. 52.5-53.5° (from a mixture of ether and *n*-pentane).





3,5-Dimethyl-4-benzoyloxazole. a) To 7 g of phenyl-(3,5-dimethylisoxazolyl-4)-chloromethane was added a solution of 15 g of potassium bichromate in 70 ml of water, and 35 ml of concentrated sulfuric acid was introduced dropwise. When spontaneous boiling of the reaction mixture ceased, the latter was heated for a further 5 min, cooled, poured into water, and neutralized with potassium carbonate. The precipitate was removed by filtration and treated several times with hot benzene. Removal of the solvent yielded 3.75 g (59%) of 3,5-dimethyl-4-benzoylisoxazole with m. p. 60-61°.

b) To a solution of 0.55 g of phenyl-(3,5-dimethylisoxazolyl-4)-carbinol in 10 ml of acetic acid was added a solution of 0.76 g of chromic anhydride in 1 ml of water. The solution was boiled under reflux for 1 hr and diluted with water to liberate an oil, which crystallized after a few days. We obtained 0.35 g of 3,5-dimethyl-4-benzoylisoxazole with m. p. 61-62°, which did not depress the melting point of the sample obtained by method "a". After three recrystallizations from benzene, the ketone had m. p. 62-63°. 3,5-Dimethyl-4-benzoylisoxazole formed colorless crystals, which were readily soluble in ether and chloroform and stable during storage.

Found %: C 71.91, 72.16; H 5.24, 5.44; N 6.69, 6.70.  $C_{12}H_{11}O_2N$ . Calculated %: C 71.62; H 5.51; N 6.96.

3,5-Dimethyl-4-(p-carboxybenzoyl)-isoxazole. To 3.6 g of p-tolyl-(3,5-dimethylisoxazolyl-4)-chloromethane was added a solution of 7.2 g of potassium bichromate in 35 ml of water, and 17 ml of concentrated sulfuric acid was introduced dropwise. The reaction mixture evolved heat and boiled; it was boiled for 1 hr, cooled, and diluted with an equal volume of water. The precipitate was collected and dissolved in boiling acetic acid. Cooling the solution yielded 1.7 g of 3,5-dimethyl-4-(p-carboxybenzoyl)-isoxazole, which had m. p. 196-197° (in a sealed capillary) after two recrystallizations from acetic acid. The colorless crystalline substance partly sublimed on heating. It was readily soluble in acetone, sparingly soluble in ether, benzene, and chloroform, and insoluble in water. It was stable during storage.

Found %: N 5.93, 5.90.  $C_{13}H_{11}O_4N$ . Calculated %: N 5.71.

3-Benzyl-2,4-pentanedione. Into a three-necked flask with a stirrer and reflux condenser were placed 100 g of acetylacetone, 126 g of benzyl chloride, 70 g of potassium carbonate, and 100 ml of water, the mixture boiled for 4 hr with vigorous stirring, and then the aqueous layer separated and extracted with ether. The organic layer and ether extracts were dried over magnesium sulfate, the solvent and unreacted starting materials removed by distillation, and the residue was vacuum distilled. We obtained 58 g (30% on the acetylacetone taken and 51% on that reacting) of 3-benzyl-2,4-pentanedione.

b. p. 135-136° (7 mm),  $n_D^{20}$  1.5306,  $d_4^{20}$  1.059. Literature data: b. p. 143-146° (10 mm) [8],  $d_4^{20}$  1.063 [9].

3,5-Dimethyl-4-benzylisoxazole. a) Into a three-necked flask with a stirrer and reflux condenser was placed a solution of 20 g of phenyl-(3,5-dimethylisoxazolyl-4)-chloromethane in 75 ml of glacial acetic acid. To the boiling reaction mixture was added 20 g of zinc dust in small portions. The reaction mixture was heated and stirred for 2 hr, poured into water, and neutralized with potassium carbonate and the excess zinc removed by filtration and washed with chloroform on the filter. The filtrate was extracted with chloroform, the combined extracts were dried over calcium chloride, the solvent was removed, and the residue fractionated in vacuum. We obtained 6.4 g (38%) of 3,5-dimethyl-4-benzylisoxazole with b. p. 95° at 0.5 mm. The chloroferrate, which was obtained by a known procedure [10], had m. p. 75-76°.

b) Over a period of 1 hr, an aqueous solution of 25 g of hydroxylamine hydrochloride neutralized with potassium carbonate was added dropwise to 33 g of 3-benzyl-2,4-pentanedione heated on a boiling water bath. The mixture was then heated for a further 4 hr, cooled, and extracted with chloroform and the extract dried over calcium chloride. The solvent was removed and the residue vacuum distilled. We obtained 15 g (46%) of 3,5-dimethyl-4-benzylisoxazole with b. p. 95-97° (0.5 mm). After redistillation, the product had b. p. 95° (0.5 mm),  $n_D^{20}$  1.5365,  $d_4^{20}$  1.066.

Found %: N 7.13, 7.14.  $C_{12}H_{13}ON$ . Calculated %: N 7.48.

The colorless, oily liquid with a weak odor was miscible with organic solvents and stable during storage.

The chloroferrate of 3,5-dimethyl-4-benzylisoxazole had m. p. 76-77° and did not depress the melting point of the chloroferrate of the sample obtained by method "a."

**Condensation of phenyl-(3,5-dimethylisoxazolyl-4)-chloromethane with  $\beta$ -dimethylaminoethanol.** A solution of 23.5 g of phenyl-(3,5-dimethylisoxazolyl-4)-chloromethane in 20 ml of dimethylaminoethanol was added dropwise with stirring and cooling in a mixture of ice and salt to a solution prepared from 2.44 g of sodium and 60 ml of  $\beta$ -dimethylaminoethanol. The cooling mixture was removed and the reaction mixture stirred at room temperature for 4 hr. It was then diluted with 100 ml of absolute ether, the precipitate of sodium chloride removed by filtration, and the solvent and excess aminoethanol were removed by distillation. The residue partly crystallized on standing in a refrigerator. We obtained 5.3 g of 1,2-diphenyl-1,2-di-(3',5'-dimethylisoxazolyl-4')-ethane with m. p. 196-197°. After recrystallization from aqueous methanol, the substance had m. p. 206°. The fine, colorless crystals were soluble in benzene, methanol, acetone, and dichloroethane, insoluble in ether and ligroin, and stable during storage.

Found %: C 77.97; H 6.03 (the substance burned with explosions); N 7.27, 7.57.  $C_{24}H_{24}O_2N_2$ . Calculated %: C 77.39; H 6.49; N 7.52.

Vacuum distillation of the filtrate yielded 3.85 g of the starting chloride with b. p. 126-130° (1 mm),  $n_D^{20}$  1.5550.

### SUMMARY

1. The reaction of 3,5-dimethylisoxazole with aromatic aldehydes was studied, and it was shown that the methyl groups do not participate in the condensation, which proceeds through the hydrogen atoms at carbon atom 4 of the isoxazole nucleus. This condensation is a new example of electrophilic substitution in the isoxazole series.

2. We studied some reactions of the aryl-(3,5-dimethylisoxazolyl-4)-chloromethanes obtained, in particular, their hydrolysis to yield arylcarbinols and oxidation to ketones.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. Some or all of this periodical literature may well be available in English translation. A complete list of the cover-to-cover English translations appears at the back of this issue.

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## STERIC STRUCTURE AND REACTIVITY

### XVIII. INTERACTION OF REMOTE ATOMIC GROUPINGS ACCORDING TO KINETIC DATA ON THE REACTIONS OF AMINO DERIVATIVES OF DIPHENYL OXIDE, SULFIDE, AND SELENIDE WITH PICRYL CHLORIDE

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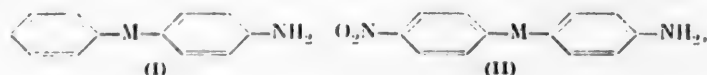
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In previous communications in this series [1-3], the results of investigating the kinetics of the reaction of p-nitrobenzoyl chloride with amino derivatives of the structures (I) and (II) in benzene were presented.



where M is an oxygen or sulphur bridging atom. It was shown that the effect of the nitro group on the rate of acylation of the amino group in the molecular systems (III) is appreciably greater than in the case of the biphenyl system (IV),



where there is no bridge separating the benzene nuclei. It was found that a more or less quantitative characteristic of the capacity for transmitting the intereffect of the  $\text{NO}_2$  and  $\text{NH}_2$  groups in the molecular systems of type (III) and (IV) is the ratio of the rate constants for the reactions of mono- and disubstituted derivatives, for example,  $K_I/K_{II}$  (f factor).

In the present communication we present data on the kinetics of analogous reactions of amino derivatives of diphenyl oxide and sulfide with picryl chloride under exactly the same conditions as previously, and these confirmed previous observations by kinetic results for a reaction which is particularly sensitive to structural changes in the molecules of the aromatic amino derivatives [4]. To complete the picture, we prepared similar derivatives of diphenyl selenide and also studied their reactivity toward picryl chloride.

## EXPERIMENTAL

### I. Preparation and Purification of Starting Materials

Benzene and picryl chloride [4] were purified as reported previously. 4-Aminodiphenyl oxide (I, M = O), 4-amino-4'-nitrodiphenyl oxide (II, M = O), and 4-aminodiphenyl sulfide (I, M = S) were prepared and purified as described in our articles [1, 2]. 4-Amino-4'-nitrodiphenyl sulfide (II, M = S) was prepared by partial reduction of 4,4'-dinitrodiphenyl sulfide both with sodium disulfide [2] and by the method described below for the preparation of the analogous aminonitro derivative of diphenyl selenide.

4-Aminodiphenyl selenide\* was prepared [5] by heating phenylseleninic acid [6] with aniline. The authors of [5] recommended that the excess aniline be removed by steam distillation after the reaction and the product extracted from the residue with hydrochloric acid. In this case the amine was very impure and had a violet color due to impurities, which were difficult to remove from it. We found that it was best to raise the steam temperature to 150° after distillation of the aniline. Under these conditions, almost colorless 4-aminodiphenyl selenide distilled readily and its further purification presented no difficulties. For this purpose the amine was converted to the salt and recrystallized five times from 10% sulfuric acid (at first with activated charcoal). The free base was liberated by gently heating the salt with a small amount of aqueous ammonia (careful grinding) and this was recrystallized three times from aqueous methanol (3:1) and finally from a mixture of ligroin and benzene (2:1). After being dried in vacuum for 2-3 hr at 80°, the product had m. p. 94°, which corresponds to literature data [5].

4,4'-Dinitrodiphenyl selenide. To prepare this compound, we used Matti's procedure [7], into which a number of changes and refinements were introduced. A mixture of 6 g of metallic selenium and 9 g of solid potassium hydroxide was fused in a refractory tube for 2 hr with periodic stirring at 140° (in the bath). The dark red melt formed (rapidly solidifying on cooling) was washed with several portions of cold water (a total of 100 ml) into a solution of 40 g of p-nitrochlorobenzene in 300 ml of ethanol. The mixture obtained was boiled under reflux with periodic shaking for 7 hr. The precipitate which formed on cooling was collected, dried, and dissolved in dichloroethane. By filtration of this solution we separated about 4 g of unbound selenium (cf. [8]), which was quite suitable for repeat operations, and after evaporation of the solvent the solid crystalline product was treated with steam to remove unreacted p-nitrochlorobenzene. The residue, which consisted of impure 4,4'-dinitrodiphenyl selenide (4.5 g, m. p. 98-100°), was chromatographed in benzene solution on alumina (100 ml of benzene per g of nitro compound and elution with the same solvent) and then recrystallized from ethyl acetate. The m. p. was 169-171°.

4-Amino-4'-nitrodiphenyl selenide (II, M = Se). A mixture of 2 g of 4,4'-dinitrodiphenyl selenide,\*\* 20 g of p-dichlorobenzene, and 2 ml of phenylhydrazine was heated on a paraffin bath with the temperature gradually raised [9]. Reduction began at 135° and was complete after 4-5 hr at 170° (the course of the reaction was followed by the rate of evolution of nitrogen bubbles), and then the whole mixture was dissolved in a sufficient amount of benzene and a stream of dry hydrogen chloride passed through the solution. The precipitate of the hydrochloride was collected, washed carefully with benzene, and then dissolved in the minimal amount of hot 10% sulfuric acid. The sulfate obtained on cooling the solution was recrystallized twice from 10% sulfuric acid (activated charcoal). The yield of the sulfate was 2.1 g (~100%). Grinding the salt with warm aqueous ammonia yielded the free base, which was orange. This was chromatographed in a mixture of benzene and ligroin (1:1) on alumina and the product eluted with benzene. The amine was then recrystallized successively from methanol, n-butanol, and benzene. After being dried in vacuum at 100°, the product had m. p. 123-124°.

Found %:  $\text{NH}_2$  [10] 5.46, 5.48.  $\text{C}_{12}\text{H}_{10}\text{O}_2\text{N}_2\text{Se}$ . Calculated %:  $\text{NH}_2$  5.47.

For identification purposes, the 4-amino-4'-nitrodiphenyl selenide, which has not been described in the literature, was reduced with hydrazine hydrate in alcohol in the presence of Raney nickel [11] (cf. [1, 9, 12, 13]) to 4,4'-diaminodiphenyl selenide, which has been described previously [7], and the latter was heated with a mixture of equal volumes of glacial acetic acid and acetic anhydride for 2 hr at 100° (the product was isolated by pouring the reaction mixture into water and recrystallized from dilute acetic acid) to yield the diacetyl derivative, which is also known [7].

## II. Kinetic Measurement Procedure and Results

The procedure for measuring the reaction rates and also the methods of calculating the second order rate constants, Arrhenius activation energies ( $E_A$ ), frequency factors ( $A$ ), and activation entropies ( $\Delta S^\ddagger$ ) were described previously [14]. In all experiments the initial picryl chloride concentration ( $a$ ) was half the initial amine concentration ( $b$ ).

The results obtained on the kinetics of the reactions studied are given in Tables 1-6, where  $k$  (liters/mole·sec) is the mean value of the rate constants with  $k_1$  that for the given time interval  $t_1$  for  $n_1$  measurements and

\* The student V. M. Zikranets helped with the synthesis of amino derivatives of diphenyl selenide.

\*\* The same results were obtained with the product which had been purified by chromatography alone and with the sample which had also been recrystallized from ethyl acetate.

TABLE 1

Kinetics of the Reaction of 4-Aminodiphenyl Oxide with Picryl Chloride ( $a = 0.0025$  M;  $b = 0.005$  M)

25°				50°			
$t_i$ (min)	Yield (%)	$k_i$ (liter/ mole · sec)	$n_i$	$t_i$ (min)	Yield (%)	$k_i$ (liter/ mole · sec)	$n_i$
3	20.1	0.281	2	2	33.6	0.875	1
5	29.7	0.283	3	3	41.3	0.810	2
10	45.1	0.276	3	5	55.8	0.870	2
15	57.6	0.304	4	7	64.7	0.905	2
28	70.5	0.286	3	10	71.3	0.858	2
$k_{25^\circ} = 0.288 \pm 0.007$				$k_{50^\circ} = 0.862 \pm 0.037$			

$$E_A = 8400 \text{ cal/mole}; \log A = 5.60; \Delta S^\ddagger = -35.0 \text{ cal/deg} \cdot \text{mole}$$

TABLE 2

Kinetics of the Reaction of 4-Amino-4'-Nitrodiphenyl Oxide with Picryl Chloride ( $a = 0.0025$  M;  $b = 0.005$  M)

25°				50°			
$t_i$ (min)	Yield (%)	$k_i$ (liter/ mole · sec)	$n_i$	$t_i$ (min)	Yield (%)	$k_i$ (liter/ mole · sec)	$n_i$
60	22.8	0.0165	2	14	20.4	0.0633	2
80	31.1	0.0189	2	23	28.9	0.0586	1
120	38.9	0.0178	2	39	38.3	0.0549	2
230	56.5	0.0189	2	60	51.7	0.0616	2
350	66.4	0.0189	3	120	67.6	0.0585	2
$k_{25^\circ} = 0.0183 \pm 0.0008$				$k_{50^\circ} = 0.0595 \pm 0.0028$			

$$E_A = 9100 \text{ cal/mole}; \log A = 4.91; \Delta S^\ddagger = -38.0 \text{ cal/deg} \cdot \text{mole}$$

TABLE 3

Kinetics of the Reaction of 4-Aminodiphenyl Sulfide with Picryl Chloride ( $a = 0.005$  M;  $b = 0.01$  M)

25°				50°			
$t_i$ (min)	Yield (%)	$k_i$ (liter/ mole · sec)	$n_i$	$t_i$ (min)	Yield (%)	$k_i$ (liter/ mole · sec)	$n_i$
12	13.7	0.0211	1	7	22.5	0.0716	1
21	20.6	0.0207	3	14	40.2	0.0830	2
36	29.5	0.0195	2	20	45.6	0.0724	2
50	39.0	0.0215	2	27	53.5	0.0737	2
83	50.9	0.0209	2	50	70.8	0.0839	2
155	65.7	0.0207	2				
$k_{25^\circ} = 0.0208 \pm 0.007$				$k_{50^\circ} = 0.0775 \pm 0.0048$			

$$E_A = 10100 \text{ cal/mole}; \log A = 5.70; \Delta S^\ddagger = -34.5 \text{ cal/deg} \cdot \text{mole}$$

TABLE 4

Kinetics of the Reaction of 4-Amino-4'-nitrodiphenyl Sulfide with Picryl Chloride  
(a = 0.005 M; b = 0.01 M)

25°				50°			
$t_i$ (min)	Yield (%)	$k_i$ (liter/ mole · sec)	$n_i$	$t_i$ (min)	Yield (%)	$k_i$ (liter/ mole · sec)	$n_i$
244	8.63	0.000650	2	120	17.7	0.00341	2
420	13.3	0.000643	2	193	27.6	0.00341	2
793	23.9	0.000665	2	305	36.0	0.00318	1
1390	36.7	0.000699	2	550	52.9	0.00353	2
2100	48.0	0.000736	3	840	64.3	0.00370	2
$k_{25^\circ} = 0.000678 \pm 0.000046$				$k_{50^\circ} = 0.00341 \pm 0.00020$			

$$E_A = 12400 \text{ cal/mole; } \log A = 5.90; \Delta S^\ddagger = -33.6 \text{ cal/deg} \cdot \text{mole}$$

TABLE 5

Kinetics of the Reaction of 4-Aminodiphenyl Selenide with Picryl Chloride  
(a = 0.005 M; b = 0.01 M)

25°				50°			
$t_i$ (min)	Yield (%)	$k_i$ (liter/ mole · sec)	$n_i$	$t_i$ (min)	Yield (%)	$k_i$ (liter/ mole · sec)	$n_i$
12	18.0	0.0305	2	5	22.1	0.0979	2
22	27.3	0.0288	2	10	36.0	0.0965	2
36	35.8	0.0260	2	11	37.9	0.0956	1
60	49.8	0.0277	2	20	53.4	0.0990	2
				30	61.7	0.0926	2
$k_{25^\circ} = 0.0283 \pm 0.0016$				$k_{50^\circ} = 0.0964 \pm 0.0033$			

$$E_A = 9300 \text{ cal/mole; } \log A = 5.26; \Delta S^\ddagger = -36.5 \text{ cal/deg} \cdot \text{mole}$$

TABLE 6

Kinetics of the Reaction of 4-Amino-4'-nitrodiphenyl Selenide with Picryl Chloride  
(a = 0.005 M; b = 0.01 M)

25°				50°			
$t_i$ (min)	Yield (%)	$k_i$ (liter/ mole · sec)	$n_i$	$t_i$ (min)	Yield (%)	$k_i$ (liter/ mole · sec)	$n_i$
210	15.0	0.00141	1	60	18.5	0.00656	2
213	13.1	0.00119	1	105	25.4	0.00559	3
472	24.8	0.00117	2	180	37.6	0.00578	2
595	34.4	0.00141	2	334	57.1	0.00687	2
880	39.2	0.00123	2	618	67.8	0.00587	2
1443	51.9	0.00124	2				
$k_{25^\circ} = 0.00127 \pm 0.00008$				$k_{50^\circ} = 0.00608 \pm 0.00036$			

$$E_A = 12100 \text{ cal/mole; } \log A = 5.94; \Delta S^\ddagger = -33.4 \text{ cal/deg} \cdot \text{mole}$$



k for all  $\epsilon n_1$  measurements. The mean value of the reaction yield for  $n_1$  measurements is given in the second column. Table 7 is a summary.

## DISCUSSION OF RESULTS\*

A comparison of the rates of reaction of aniline, 4-aminobiphenyl, and amines with bridging heteroatoms of the type  $p\text{-C}_6\text{H}_5\text{MC}_6\text{H}_4\text{NH}_2$  shows that the para substituents introduced into the aniline molecule may be arranged in the following series with respect to the decrease in the electron-donor (and increase in electron-acceptor) properties:



The members of this series lying to the left of H are donors and those lying to the right are acceptors of electrons.





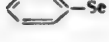

It is interesting that in the series of substituents  $\text{C}_6\text{H}_5\text{O}$ ,  $\text{C}_6\text{H}_5\text{S}$  and  $\text{C}_6\text{H}_5\text{Se}$ , where the heteroatoms belong to the same group of the Periodic Table, the electronic effect of the substituent changes sharply from the first to the second member of this series, while the S- and Se-containing substituents behave practically the same in this respect. Similar phenomena are also observed on comparing the reactivity of some other compounds containing analogous groups. For example, there is a very similar relation between values of the Hammett constants\*\*  $\sigma$  of the groups [16]  $p\text{-CH}_3\text{O}$ -,  $p\text{-CH}_3\text{S}$ - and  $p\text{-CH}_3\text{Se}$ - or a series of other para substituents in which the nature of the heteroatom is varied within the same group of the Periodic System [16]. This peculiarity in the properties of the substituents  $\text{C}_6\text{H}_5\text{O}$ -,  $\text{C}_6\text{H}_5\text{S}$ - and  $\text{C}_6\text{H}_5\text{Se}$ - is most probably explained by the presence of d-electron orbitals in sulfur and selenium atoms and their participation in conjugation with the  $\pi$ -electron system of the aromatic nucleus, while oxygen atoms do not have these orbitals (see below for details).

As has already been pointed out above, the degree of transmission of the interaction of substituents from one benzene nucleus to another in molecular systems of the type (III) and (IV) may be assessed by means of the ratio of the rate constants for the reactions of mono- and disubstituted derivatives ( $f$  factor). Table 8 gives the values of  $f$ , which show that in all the molecular systems with bridging heteroatoms, the effect of the nitro group on the reactivity of the amino group increases with a change from diphenyl oxide to diphenyl sulfide and then decreases slightly in the case of the molecular system of diphenyl selenide\*\*\* and again increases strongly in the diphenylamine system. There is every reason to think [15] that the values of  $f$  more or less quantitatively reflect the transmission of the electronic interaction of the substituents from one benzene nucleus through the bridging heteroatom. It should be emphasized in particular that the introduction of a heteroatom between the

\* See summary in Table 7.

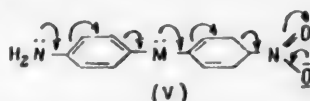
\*\* These constants are a measure of the electronic effect of a substituent on the reactivity of some functional group attached to an aromatic nucleus [16-18].

\*\*\* It is interesting to note that according to spectrophotometric data on furans, thiophenes, and selenophenes [19], the conjugation of the unshared pair of p-electrons of the heteroatom with the  $\pi$ -electrons of the carbon atoms is in the same order as the value of  $f$  for the molecular systems we studied. We should also point out that the melting points of the amino derivatives studied increase with a change from oxygen-containing compounds to their sulfur analogs and again fall with selenium derivatives, as is indicated by data in the table below.

R in $\text{R}-\text{C}_6\text{H}_4-\text{NH}_2$	M.p.	R in $\text{R}-\text{C}_6\text{H}_4-\text{NH}_2$	M.p.
	85°		134°
	97		145
	94		124

Thus, there is a quite definite analogy between the properties of the compounds we examined with bridging heteroatoms and the properties of heterocyclic substances containing the same heteroatoms, though in the first case the heteroatoms do not form part of a cyclic system (cf. [14]).

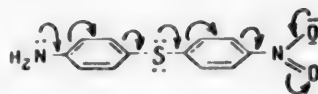
benzene nuclei, together with separating these nuclei in comparison with their disposition in the molecular system of biphenyl, leads to a strengthening rather than a weakening of the transmission of the effect of the nitro group on the reactivity of the amino group. In all cases, the factor  $f$  for molecular systems with bridging heteroatoms is greater than in the case of the biphenyl system. The characteristic of these systems with bridging heteroatoms is the fact that all these heteroatoms have in their valence shells unshared pairs of  $p$ -electrons which are capable of interacting with the  $\pi$ -electron system of the benzene nuclei. This is evidently the main reason for the observed peculiarity in the properties of the system examined. In actual fact, if the two benzene nuclei are connected by a carbon bridging atom, then here the normal effect is observed and appears as a weakening of the transmission of the effect of the nitro group on the amino group due to the increase in the distance between them:  $f$  for the diphenylmethane system is appreciably less than in the case of biphenyl. Thus, it may be considered that the ready transmission of the effect of 4,4'-substituents in molecular systems with bridging heteroatoms is caused by  $p, \pi$ -conjugation of the form:



As a result of this conjugation an effective positive charge ( $+\delta$ ) should arise on the heteroatom and this is actually confirmed by experiment. All the substituents  $O_2N-C_6H_4-\ddot{M}-C_6H_4-NH_2$  with a heteroatom  $M$  have electron-acceptor properties.

Thus, with the introduction of heterobridges between two benzene nuclei we encounter a new effect, namely an increase in the interaction of 4,4'-substituents with an increase in the distance between them. This effect may be called a positive bridge effect. In contrast to the positive bridge effect, which is caused by the presence of a bridging heteroatom with  $p$ -electrons, when the benzene nuclei are connected by atoms or atomic groupings which act as insulators in the transmission of the effect of substituents from one nucleus to the other [14, 15, 20-22], we will talk of a negative bridge effect. The positive bridge effect is clearly observed in kinetic studies of molecular systems of a similar type, but is usually not confirmed by data from physical investigation methods [1-3, 5], which is most probably caused by the dominating role of dynamic factors in the conjugation of the heteroatoms with the benzene nuclei in the systems examined during a chemical conversion [23, 24].

The next problem is to attempt to explain why the values of  $f$  for the molecular systems studied change in relation to the nature of the heteroatom in the order given in Table 8. For this purpose it is necessary to compare molecular systems in which the heteroatoms are neighbors either in a group or period of the Periodic Table. In the molecular systems of diphenylamine and diphenyl oxide, the N and O atoms are neighbors in a period in the table. The first system transmits the electronic effects of the substituents better, probably due to the fact that the lability of the unshared pair of  $p$ -electrons at the nitrogen atom must be higher than at the oxygen atom (see [24], pp. 15, 61, 63, and 74) when the compounds of these elements are exactly analogous. The considerable increase in the capacity to transmit the electronic interaction of 4,4'-substituents in molecular systems with bridging atoms of the same group (O, S, and Se) with a change from the diphenyl oxide system to the diphenyl sulfide system is apparently explained by the fact that not only the  $p$ - but also the  $d$ -electrons [25] (see [24], p. 83) of the sulfur atom may participate in the conjugation with the  $p$ -electrons of the benzene nucleus, i.e., there is a tendency for the expansion of the valence shell of sulfur to ten electrons [26]. As a result of this, particularly favorable conditions are created for the transmission of the electronic effect from the nitro group to the amino group in the molecular system of diphenyl sulfide according to the following mechanism:



From the above point of view, the sulfur atom in this structure is able to fulfill a double function: On the one hand, it supplies  $p$ -electrons which are displaced toward the  $\pi$ -electron shell of the benzene nucleus bearing the nitro group and on the other hand, the same sulfur atom may accept into its  $3d$ -orbital  $\pi$ -electrons of the benzene nucleus attached to the amino group. It is quite obvious that the oxygen atom will not play this part in the molecular system of diphenyl oxide as it has no  $d$ -orbital. It is probable that for the same reason, the

TABLE 7

Summarized Data on the Kinetics of the Reaction of Amines with p-Nitrobenzoyl Chloride and Picryl Chloride\*

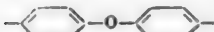
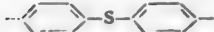


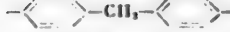

Amine	Electrophilic agent**	$k_{11}^{\circ}$	$k_{11}^{\circ}$	$E_A$	$\lg A$	$\Delta S^{\ddagger}$
	PNBC [1, 3] PC	$1.23 \pm 0.03$ $0.288 \pm 0.007$	$2.60 \pm 0.11$ $0.862 \pm 0.037$	5550 8400	4.17 5.60	-41.5 -35.0
	PNBC [1, 3] PC	$0.102 \pm 0.003$ $0.0183 \pm 0.0008$	$0.273 \pm 0.006$ $0.9595 \pm 0.0028$	7500 9100	4.53 4.91	-39.9 -38.0
	PNBC [2, 3] PC	$0.120 \pm 0.006$ $0.0208 \pm 0.007$	$0.300 \pm 0.012$ $0.0775 \pm 0.0018$	7000 10100	4.23 5.70	-41.2 -34.5
	PNBC [1, 3] PC	$0.00504 \pm 0.00018$ $0.000678 \pm 0.000046$	$0.0173 \pm 0.0008$ $0.00341 \pm 0.00020$	9700 12400	4.80 5.90	-38.5 -33.6
	PC	$0.0283 \pm 0.0016$	$0.0964 \pm 0.0033$	9300	5.26	-36.5
	PC	$0.00127 \pm 0.00009$	$0.00608 \pm 0.00036$	12100	5.94	-33.4
	PC	$2.98 \pm 0.09$	7.74	7300	5.83	-33.8
	PC	$0.0659 \pm 0.0017$	$0.214 \pm 0.004$	8700	5.20	-36.8
	PNBC PC	$0.533 \pm 0.010$ $0.0744 \pm 0.0021$	$1.11 \pm 0.02$ $0.235 \pm 0.003$	5600 8900	3.85 5.32	-42.8 -36.2
	PNBC PC	$0.0505 \pm 0.0011$ $0.00548 \pm 0.00018$	$0.118 \pm 0.003$ $0.00205 \pm 0.0009$	6500 10000	3.46 5.15	-44.7 -37.1
	PNBC PC	$0.580 \pm 0.018$ $0.120 \pm 0.002$	$0.394 \pm 0.005$	— 9100	— 5.75	— -34.3

\* The dimensions are the same as in Tables 1-6.

\*\* PNBC, p-nitrobenzoyl chloride; PC, picryl chloride.

TABLE 8

Values of  $f$  Factors for Various Molecular Systems

Molecular systems	For reactions with p-nitrobenzoyl chloride	For reactions with picryl chloride
	12.1 [1,3]	15.8
	23.8 [2,3]	30.7
	—	24.6
	—	43.3 [15]
	4.34 [20]	5.96 [20]
	10.6 [14]	13.6 [14]

molecular system of diphenyl selenide is a better transmitter of the interaction of the 4,4'-substituents than the diphenyl oxide system. The difference in the selenium-containing system and the diphenyl sulfide system apparently may be interpreted in terms of the general tendency for a decrease in the conjugation of heteroatoms with an aromatic nucleus with the substitution of one such heteroatom for its lower neighbor in the Periodic Table [26] (see [24], pp. 63 and 64) which is observed under otherwise equal conditions.

As regards the energy parameters of the reactions investigated in the present work, it may be stated that these reactions proceed with low values of  $E_A$  and  $\Delta S^\ddagger$ , and in general, the reactions of various amines are characterized by appreciably lower changes in  $\Delta S^\ddagger$  than  $E_A$ . Due to the quite complex structure of the substances participating in the reactions studied, the primary experimental data on the rate constants rather than the values of  $E_A$ ,  $A$ , and  $\Delta S^\ddagger$  should be more reliable criteria for assessing the effects of a change in the structure of the amino derivative on its reactivity [15].

The results of this work, which are based on a study of the kinetics of reactions of amino derivatives of types (I) and (II) with picryl chloride, are in complete agreement with data obtained by studying the kinetics of reactions of the same amines with p-nitrobenzoyl chloride (see Tables 7 and 8 and also [1-3]). However, the effect of successive changes in structural factors in the molecules of the amino derivatives is expressed more clearly in reactions with picryl chloride than in similar reactions with p-nitrobenzoyl chloride, and this is explained by the extremely high sensitivity of the first series of reactions toward the action of these factors [4]. As we had a limited amount of selenium-containing amines, we were unable to make a detailed study of their reactivity toward p-nitrobenzoyl chloride. However, a series of incomplete preliminary experiments with these substances showed that the conclusions of the present work were completely confirmed by kinetic data for the reactions of these amines with p-nitrobenzoyl chloride.

## SUMMARY

1. The kinetics of the reactions of 4-aminodiphenyl oxide, sulfide, and selenide and their 4'-nitro derivatives with picryl chloride in benzene were studied.

2. In the molecular systems of diphenyl oxide, sulfide, and selenide, in which the benzene nuclei are connected by bridging heteroatoms of O, S, and Se, the 4'-NO<sub>2</sub> group affects the reactivity of the 4-NH<sub>2</sub> group more strongly than in the biphenyl system, where the benzene nuclei are connected directly, and this indicates greater transmission of the electronic effects of substituents from one benzene nucleus to another in systems with bridging heteroatoms ("positive bridge effect").

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## BIS( $\beta$ -CHLOROETHYL)-AMINES OF BICYCLIC COMPOUNDS

### II. 4-METHOXY-1-BIS( $\beta$ -CHLOROETHYL)-AMINOINDAN AND CYCLIZATION OF o-METHOXYPHENYLPROPIONIC ACID

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3-Methoxy-1-bis( $\beta$ -chloroethyl)-aminoindan was not among the series of bis( $\beta$ -chloroethyl)-aminoindans described by one of us in a previous article. As a starting material for the preparation of this compound we required 4-methoxyindan-1-one, which was synthesized [1] by isomerization of dihydrocoumarin by heating with  $AlCl_3$  and subsequent methylation of the 4-hydroxyindan-1-one formed. The same ketone could be obtained by cyclization of o-methoxyphenylpropionic acid. A number of investigators [2] unsuccessfully attempted to cyclize this acid in the presence of various reagents ( $HF$ ,  $P_2O_5$ , etc.) by using both the free acid and its acid chloride in the reaction. Interesting reasons were given for the difficulty in the cyclization of this acid [2].

We attempted to cyclize o-methoxyphenylpropionic acid with polyphosphoric acid, which, according to our work, gives better results than other cyclizing agents.

In addition, we repeated experiments on the cyclization of the acid chloride by the Friedel-Crafts method in various solvents. No 4-methoxyindan-1-one was obtained in any of our experiments, but in all cases we observed the formation of an amorphous substance with m. p. 250-290°. Other authors [2] have mentioned the formation of a similar substance, but there have been no detailed investigations of this product. It was to be assumed that in our experiments, the main direction of the reaction was the formation of precisely this substance; the elucidation of its structure should help to determine the reasons for the difficulties in the cyclization of o-methoxyphenylpropionic acid to the ketone. A great hindrance to attempts to investigate this substance in more detail was its insolubility in many organic solvents, alkalis, and acids; it was found to be soluble in phenol, from which it could be recrystallized, and also in sulfuric acid, with the formation of a dark red solution. By treatment of the substance with hot chloroform, we were able to isolate a sample which melted over a narrow range (280-288°). The elementary composition of this sample corresponded to that of methoxyindanone, but the molecular weight, which was found cryoscopically in phenol, was 4 times that of methoxyindanone. We were unable to detect a carbonyl group in the substance with the normal reagents because of its insolubility in organic solvents. Only the reaction of the substance with 2,4-dinitrophenylhydrazine in sulfuric acid yielded a dark red substance, which melted at 350° and was difficult to investigate.

The infrared absorption spectra of samples of the substance obtained by the cyclization of o-methoxyphenylpropionic acid (which were in the unpurified state, had been treated with chloroform, and recrystallized from phenol) were found to be identical and indicated the presence of a carbonyl group. The results of our experiments indicate that this substance is a tetramer containing methoxyl and carbonyl groups.

We prepared the 4-methoxyindan-1-one required for our work according to literature data [1]. 4-Methoxyindan-1-one oxime was reduced to the corresponding amine. The bis- $\beta$ -chloroethyl derivative of 4-methoxy-1-aminoindan was obtained by the usual method through 4-methoxy-1-bis( $\beta$ -hydroxyethyl)-aminoindan.



In addition, for comparison with the substance obtained from 2,4-dinitrophenylhydrazine and the amorphous, high-melting substance mentioned above, we prepared the 2,4-dinitrophenylhydrazone of 4-methoxyindan-1-one, which has not been described in the literature. The properties of these hydrazones were completely different.

## EXPERIMENTAL

Attempted cyclization of o-methoxyphenylpropionic acid in the presence of polyphosphoric acid. To freshly prepared polyphosphoric acid (24 g of phosphorus pentoxide and 16 g of 85% phosphoric acid) stirred at 70° was gradually added 4 g of o-methoxyphenylpropionic acid.\* The reaction mixture was stirred at 70° for 30 min and then cooled and neutralized with 10-15% sodium carbonate solution. The precipitate liberated was collected, washed with water, and dried; it had m. p. 245-280°. We obtained 3.5 g of product. The substance was boiled repeatedly with chloroform, the chloroform solutions were combined, the chloroform was removed, and the residue recrystallized from a mixture of chloroform and benzene. We obtained a colorless substance with m. p. 280-288°, which was practically insoluble in the normal organic solvents, alkalis, and acids, sparingly soluble in chloroform, and soluble in phenol and sulfuric acid; it dissolved in the latter to form a red solution.

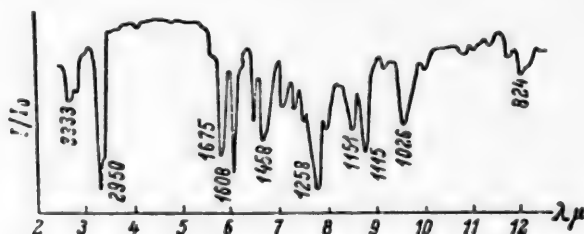
Found %: C 74.2; H 6.24; OCH<sub>3</sub> 18.48. M 652, 638, 610 (cryoscopically in phenol). C<sub>10</sub>H<sub>10</sub>O<sub>2</sub>. Calculated %: C 74.05; H 6.27; OCH<sub>3</sub> 19.13. M 648.

The spectrum\*\* showed an absorption band characteristic of the CO group in aliphatic-aromatic ketones (1680-1700 cm<sup>-1</sup>).

The reaction of 2,4-dinitrophenylhydrazine and the substance with m. p. 262-272° in sulfuric acid yielded a red, crystalline substance, which did not melt at 350°, was insoluble in alcohol and ether, but soluble in chloroform. It contained 7.01% of nitrogen.

2,4-Dinitrophenylhydrazone of 4-methoxyindan-1-one. A solution of 0.5 g of 4-methoxyindan-1-one (m. p. 102-103°) [3] in 20 ml of alcohol was added to 0.4 g of dinitrophenylhydrazine in 2 ml of conc. H<sub>2</sub>SO<sub>4</sub>, 3 ml H<sub>2</sub>O, and 10 ml of C<sub>2</sub>H<sub>5</sub>OH. An orange precipitate formed. It had m. p. 265-267° (from CHCl<sub>3</sub>). The product was a red crystalline substance.

Found %: C 55.65; H 3.98; N 15.82. C<sub>16</sub>H<sub>14</sub>O<sub>5</sub>N<sub>4</sub>. Calculated %: C 55.92; H 4.40; N 16.32.



Infrared absorption spectrum of cyclization product of o-methoxypropionic acid, recrystallized from phenol and melting at 262-272°.

4-Methoxyindan-1-one oxime. A solution of 1.72 g of hydroxylamine hydrochloride in 5 ml of water and 6 ml of a 15% solution of sodium carbonate were added simultaneously to 2 g of 4-methoxyindan-1-one in 10 ml of alcohol. The mixture was heated at 60° for 4 hr. The substance which separated was collected and washed with water to yield 1.7 g of 4-methoxyindanone oxime with m. p. 184.5-185° (from alcohol).

Found %: C 68.03; H 6.33; N 6.88. C<sub>10</sub>H<sub>11</sub>O<sub>2</sub>N. Calculated %: C 67.80; H 6.26; N 7.91.

\* We prepared o-methoxyphenylpropionic acid by catalytic hydrogenation of o-methoxyphenylacrylic acid in the presence of Raney nickel. According to literature data, the reduction has been carried out with sodium amalgam [3] or catalytically in the presence of Adams catalyst [2].

\*\* The infrared spectrum was plotted in the physicochemical laboratory of the Institute under the direction of Yu. N. Shel'ner.

4-Methoxy-1-aminoindan. To 45 g of amalgamated aluminum turnings in 300 ml of absolute ether was added 15.25 g of 4-methoxyindan-1-one oxime suspended in 2.5 liters of absolute ether. The reaction mixture was stirred at the boiling point for 30 min, and then 100 ml of water was added gradually over a period of 8 hr and the mixture left overnight. The ether solution of the amine obtained was filtered and dried with potassium carbonate, the ether removed, and the residue vacuum distilled with the amine protected from atmospheric carbon dioxide. It had b. p. 100-112° at 2.5 mm and m. p. 40-42° (in a sealed capillary).

4-Methoxy-1-aminoindan hydrochloride. The colorless crystalline substance had m. p. 222-224°.

Found %: C 60.1; H 6.95; N 7.31; Cl 17.79.  $C_{10}H_{13}ON \cdot HCl$ . Calculated %: C 60.45; H 6.60; N 7.05; Cl 17.85.

4-Methoxy-1-bis( $\beta$ -hydroxyethyl)-aminoindan hydrochloride. A mixture of 9.31 g of 4-methoxy-1-aminoindan and 6 ml of ethylene oxide was heated in a sealed tube at 135-140° for 6 hr. We obtained 12 g of an oily substance, which was soluble in benzene and chloroform and more difficultly soluble in ether. It was dissolved in absolute ether and an ether solution of hydrogen chloride added. This precipitated 4-methoxy-bis( $\beta$ -hydroxyethyl)-aminoindan hydrochloride with m. p. 130-134° (from alcohol and benzene).

Found %: N 4.96.  $C_{14}H_{21}O_3N \cdot HCl$ . Calculated %: 4.89.

4-Methoxy-1-bis( $\beta$ -chloroethyl)-aminoindan hydrochloride. To a solution of 3.3 g of 4-methoxy-1-bis( $\beta$ -hydroxyethyl)-aminoindan in 30 ml of anhydrous benzene at 8-12° was added 6 ml of thionyl chloride. The mixture obtained was stirred at room temperature for 4 hr. The solvent and excess thionyl chloride were removed by distillation. The residue was recrystallized from a mixture of benzene and alcohol, when it had m. p. 169-170°.

Found %: C 51.66; H 6.19; N 4.51; Cl 33.01.  $C_{14}H_{19}ONCl_2 \cdot HCl$ . Calculated %: C 51.78; H 6.20; N 4.32; Cl 32.76.

#### SUMMARY

4-Methoxy-bis( $\beta$ -chloroethyl)-aminoindan was synthesized, and new data were obtained on the substance formed by cyclization of o-methoxyphenylpropionic acid.

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# BIS( $\beta$ -CHLOROETHYL)-AMINOMETHYL DERIVATIVES OF AZOBENZENE

## I. METHOD OF PREPARING BIS( $\beta$ -CHLOROETHYL)-AMINES OF 4-SUBSTITUTED 4'-METHYL AZOBENZENES

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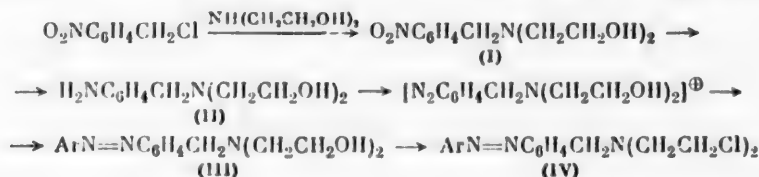
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In connection with our work on aliphatic-aromatic bis( $\beta$ -chloroethyl)-amines  $\text{Ar}-\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2\text{Cl})_2$  [1], we began an investigation of substances of this type in the azobenzene series. These compounds may be obtained by azo coupling of amines containing the group  $-\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2\text{OH})_2$  (II) with various azo components:



We chose dimethylaniline as the azo component. When our work was already complete, there appeared a communication [2] on the synthesis of the compound we prepared, namely 4-dimethylamino-4'-bis( $\beta$ -chloroethyl)-aminomethylazobenzene. However, our synthesis scheme differs somewhat from that presented in the literature [2]. The main difference between the proposed schemes is the fact that the authors of [2] replaced the hydroxyl in the hydroxyethyl groups by chlorine in compound (I), while in our scheme this replacement was carried out with compound (III); as a result of this, the diazo components in the schemes were different.

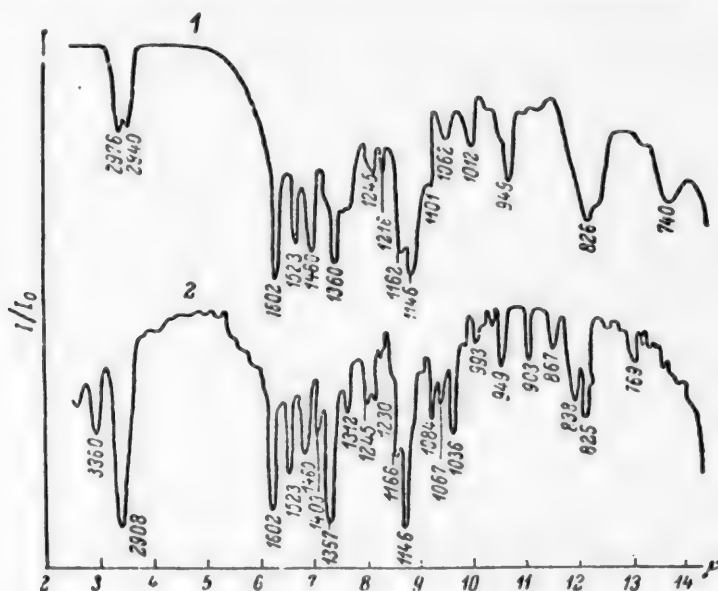
In our scheme difficulties were encountered in the reduction of the nitro group in p-nitrobenzyl-bis( $\beta$ -hydroxyethyl)-amine (I). In experiments on the catalytic hydrogenation of the nitro group of this amine in the presence of palladium or Raney nickel, 4 and not 3 moles of hydrogen were absorbed, and at the same time as reduction of the nitro group, there was destruction of the molecule with the formation of p-toluidine.

We attempted to stop the reaction after the absorption of 3 moles of hydrogen in the hydrogenation in the presence of Raney nickel, but even in this case only p-toluidine was isolated. The ease of cleavage of the p-aminobenzyl-bis( $\beta$ -hydroxyethyl)-amine molecule was confirmed by hydrogenation of this compound, which was prepared by a different method; in this case there was rapid absorption of 1 mole of hydrogen, and p-toluidine was isolated in a quantitative yield as a result of the reaction. We were able to reduce the nitro group in the nitroamine (I) selectively only by means of stannous chloride.

It is interesting to note that the same complications were encountered by the authors of [2] in the reduction of p-nitrobenzyl-bis( $\beta$ -chloroethyl)-amine, but they overcame these difficulties by using palladium of low activity as the catalyst.

We encountered no difficulties in the remaining stages of our scheme (diazotization, azo coupling, and replacement of the hydroxyl groups by chlorine atoms).

The infrared absorption spectra\* of compound (III) and (IV) were plotted (see figure), and the refractive indices of the base (IV) in benzene solutions of various concentrations were determined.



Infrared absorption spectra. 1) 4-Dimethylamino-4'-bis(β-chloroethyl)-aminomethylazobenzene; 2) 4-dimethylamino-4'-bis(β-hydroxyethyl)-aminomethylazobenzene.

#### EXPERIMENTAL

p-Nitrobenzyl-bis(β-hydroxyethyl)-amine (I). A solution of 10 g of p-nitrobenzyl chloride in 40 ml of anhydrous benzene was added with stirring to a solution of 12.2 g of diethanolamine in 25 ml of anhydrous benzene and the mixture stirred at the boiling point for 5 hr and left at room temperature for 12 hr. The benzene layer was separated from the reddish brown oil, and by rubbing the solution with a glass rod we isolated crystals of p-nitrobenzyl-bis(β-hydroxyethyl)-amine (3.4 g) with m. p. 70-73°. We obtained a further 4.5 g of nitroamine with m. p. 70-73° by mixing the remaining reddish brown oil with water. After recrystallization from benzene with activated charcoal, the substance had m. p. 75.5-77° and the yield was 7-7.8 g (50-56%). The colorless crystals were readily soluble in chloroform, acetone, and alcohol, moderately soluble in benzene and ether, and difficultly soluble in ligroin and water.

Found %: C 54.79; H 6.64; N 11.51.  $C_{11}H_{16}O_4N_2$ . Calculated %: C 54.98; H 6.71; N 11.67.

p-Nitrobenzyl-bis(β-hydroxyethyl)-amine hydrochloride was obtained by the action of an ether solution of hydrogen chloride on the amine and had m. p. 127-128°.

Found %: C 47.00; H 6.55; N 9.98; Cl 12.98, 12.92.  $C_{11}H_{16}O_4N_2 \cdot HCl$ . Calculated %: C 47.73; H 6.19; N 10.13; Cl 12.82.

p-Nitrobenzyl-bis(β-chloroethyl)-amine hydrochloride. To a solution of 6.4 g of p-nitrobenzyl-bis(β-hydroxyethyl)-amine in 35 ml of anhydrous chloroform was gradually added 30 ml of thionyl chloride and the mixture obtained heated under reflux at 70° for 4 hr. The excess thionyl chloride and chloroform were removed in vacuum. The crystalline residue with m. p. 138-143° was recrystallized from acetone with activated charcoal to give p-nitrobenzyl-bis(β-chloroethyl)-amine hydrochloride with m. p. 147-148°. The colorless crystals

\* The spectra were plotted in the physicochemical laboratory of the All-Union Chemicopharmaceutical Scientific Research Institute under the direction of Yu. N. Sheinker.

were readily soluble in methanol and ethanol and difficultly soluble in water, ether, ethyl acetate, chloroform, and benzene. The yield was close to quantitative.

Found %: C 41.79; H 4.68; N 8.93; Cl<sup>-</sup> 11.32, 11.27.  $C_{11}H_{14}O_2N_2Cl_2 \cdot HCl$ . Calculated %: C 42.15; H 4.82; N 8.93; Cl<sup>-</sup> 11.30.

Hydrogenation of p-nitrobenzyl-bis(β-hydroxyethyl)-amine. a) Over palladium chloride. A mixture of 6.8 g of p-nitrobenzyl-bis(β-hydroxyethyl)-amine hydrochloride, 100 ml of rectified alcohol, and a solution of palladium chloride in hydrochloric acid (obtained by heating 1.52 g of PdCl<sub>2</sub> in 7.95 ml of 12% hydrochloric acid) was shaken in a hydrogen atmosphere at a pressure of 70-80 cm of water. Over a period of 5.5 hr, 2760 ml of hydrogen was absorbed, and this corresponds to approximately 4 moles (2658 ml at 20° and 751 mm). The slight excess of the hydrogen volume actually absorbed over that calculated is explained by the absorption of hydrogen during the formation of palladium black. The catalyst was separated from the alcohol solution by filtration, the filtrate evaporated to dryness, excess concentrated sodium hydroxide solution added to the residue, and the mixture steam distilled. In the distillate we obtained the theoretical amount of p-toluidine with m. p. 43-44.5°, which was identified as the acetyl derivative with m. p. 146.5-147°.

b) Over Raney nickel. A mixture of 5 g of p-nitrobenzyl-bis(β-hydroxyethyl)-amine, 100 ml of methanol, and 5 g of Raney nickel was shaken with hydrogen at a pressure of 70-80 cm of water at room temperature. When the hydrogenation rate fell, catalyst was added (after the absorption of 925 ml in one experiment), and after the absorption of 1500 ml of hydrogen, a further 5 g of catalyst was added. After hydrogenation for 13 hr, 1890 ml of hydrogen had been absorbed, and this corresponds approximately to 4 moles (2070 ml at 751 mm). The methanol solution was filtered free from catalyst and evaporated to dryness in vacuum, concentrated sodium hydroxide solution added, and the mixture steam distilled. The p-toluidine distilling (m. p. 45°) was identified as the acetyl derivative (m. p. 146.5-147°).

If hydrogenation was carried out until 3 moles of hydrogen (1555 ml) had been absorbed and the reaction stopped, the reaction mixture was also found to contain p-toluidine.

p-Aminobenzyl-bis(β-hydroxyethyl)-amine (II). Stannous chloride (14.35 g) was dissolved in 22 ml of concentrated hydrochloric acid (d 1.19) at 120° (in a bath). The solution was then cooled to room temperature and 15 ml of alcohol added with cooling. To the solution was added 5.53 g of p-nitrobenzyl-bis(β-hydroxyethyl)-amine hydrochloride and the mixture heated at 110-120° (in the bath) for 2 hr. The reaction mixture was evaporated in vacuum, the residue treated with 90 ml of a 50% aqueous solution of potassium carbonate, and the brownish yellow oil liberated extracted repeatedly with chloroform. The chloroform extract was dried with potassium carbonate and evaporated in vacuum at 40°. The yield was 3.57 g (84.9%). The yellowish brown oil was readily soluble in chloroform, acetone, and alcohol, and had  $n_D^{20}$  1.5718. The substance obtained was suitable for subsequent conversions without additional purification.

Found %: C 62.16; H 8.63; N 13.30.  $C_{11}H_{16}O_2N_2$ . Calculated %: C 62.82; H 8.63; N 13.33.

p-Aminobenzyl-bis(β-hydroxyethyl)-amine (3.2 g) was distilled rapidly at a pressure of 0.03-0.05 mm. We obtained 2.66 g of a substance with b. p. 169-171° (0.036 mm), 174° (0.051 mm),  $n_D^{20}$  1.5743-1.5759. Partial polymerization of the substance was observed during distillation. The fraction with  $n_D^{20}$  1.5758 was chemically pure material.

Found %: C 62.97; H 8.49; N 13.06.  $C_{11}H_{16}O_2N_2$ . Calculated %: C 62.82; H 8.63; N 13.33.

The dipicrate was obtained by the action of an alcohol solution of picric acid on the base and had m. p. 73-74.5°.

Found %: C 41.51; H 3.84; N 16.99.  $C_{11}H_{16}O_2N_2 \cdot 2C_6H_3O_2N_3$ . Calculated %: C 41.33; H 3.62; N 16.75.

Catalytic hydrogenation of p-aminobenzyl-bis(β-hydroxyethyl)-amine. A mixture of 3.15 g of p-aminobenzyl-bis(hydroxyethyl)-amine, 50 ml of alcohol, and a solution of palladium chloride in hydrochloric acid (0.74 g of PdCl<sub>2</sub> in 3.9 ml of 12% hydrochloric acid) was shaken in a hydrogen atmosphere at a pressure of 70-80 cm of water. After 105 min, 1 mole of hydrogen had been absorbed (475 ml at 20°). The catalyst was separated from the aqueous alcohol solution by filtration, the filtrate evaporated to dryness, excess concentrated sodium hydroxide solution added to the residue, and the mixture steam distilled. p-Toluidine (1.7 g) was distilled.

4-Dimethylamino-4'-bis( $\beta$ -hydroxyethyl)-aminomethylazobenzene (III). A solution of 0.62 g of sodium nitrite in 15 ml of water was added to a solution of 1.84 g of p-aminobenzyl-bis( $\beta$ -hydroxyethyl)-amine in 7.7 ml of 14.6% hydrochloric acid at 0° with vigorous stirring. The solution obtained was stirred for 30 min and added at -5° with stirring to a solution of 1.07 g of dimethylaniline in 10 ml of methanol. The reaction mixture was stirred for 30 min and then made alkaline with 5.4 ml of a 20% aqueous solution of ammonia. The oil liberated rapidly changed to scaly crystals, which were soluble in ether and mineral acids. The reaction product was extracted with ether, the extract dried with potassium carbonate, and the ether removed in vacuum. The yield was 2.5 g and the m. p. 92-93°. In the infrared absorption spectrum (see figure) the characteristic bands of the substance lay at 3360, 903, 867, 883 and 769  $\text{cm}^{-1}$ .

Found %: C 66.70; H 7.55; N 16.14.  $\text{C}_{19}\text{H}_{26}\text{O}_2\text{N}_4$ . Calculated %: C 66.64; H 7.65; N 16.37.

4-Dimethylamino-4'-bis( $\beta$ -chloroethyl)-aminomethylazobenzene (IV). To a mixture of 3.42 g of substance (III) and 103 ml of chloroform was added 14.2 ml of thionyl chloride in several portions and the mixture heated at 80° for 3 hr. The chloroform and excess thionyl chloride were then removed in vacuum at 50°, absolute ether added to the residue, and the precipitate collected and dried in a vacuum desiccator over  $\text{P}_2\text{O}_5$  and NaOH. The extremely hygroscopic, vitreous, friable, red-violet mass obtained (5.18 g) was dissolved in dilute hydrochloric acid. The solution was treated with a 50% aqueous solution of potassium carbonate, the liberated oil extracted repeatedly with ether, and the extract dried with potassium carbonate and evaporated in vacuum. The residue (3.25 g) was dissolved in 325 ml of anhydrous benzene and the solution passed through a column of chromatographic grade alumina (TU MKhp 2962-51) 9 cm long and 20 mm in diameter at a rate of 1-2 drops per second. After the benzene solution had been passed, the adsorbent was washed six times with 25-ml portions of anhydrous benzene, with the eluate collected separately. Evaporation of the main solution and the wash benzene separately yielded 1.65 g (43.5%) and 0.2 g (0.5%), respectively, of 4-dimethylamino-4'-bis( $\beta$ -chloroethyl)-aminomethylazobenzene as an oil which crystallized slowly. The infrared absorption spectrum of the substance (see figure) had characteristic bands at 1012 and 740  $\text{cm}^{-1}$ . 4-Dimethylamino-4'-bis( $\beta$ -chloroethyl)-aminomethylazobenzene was also characterized by the definite dependence of the refractive index  $n_D^{20}$  of its benzene solutions on concentration.

Concentration of substance (weight %)	$n_D^{20}$
11.18	1.5256
11.62	1.5274
20.96	1.5448
22.24	1.5520
24.80	1.5559
31.93	1.5687
55.75	1.6258

Found %: C 60.39; H 6.08; Cl 18.70.  $\text{C}_{19}\text{H}_{24}\text{N}_4\text{Cl}_2$ . Calculated %: C 60.15; H 6.38; Cl 18.70.

Dihydrochloride. A solution of 1.55 g of the base (IV) in absolute ether was made acid to Congo with an ether solution of hydrogen chloride. We obtained 1.5 g of an extremely hygroscopic red substance with m. p. 115-117° (decomp., sealed capillary).

Found %: C 49.82; H 6.07.  $\text{C}_{19}\text{H}_{24}\text{N}_4\text{Cl} \cdot 2\text{HCl}$ . Calculated %: C 50.40; H 5.77.

#### SUMMARY

4-Dimethylamino-4'-bis( $\beta$ -chloroethyl)-aminomethylazobenzene was prepared from p-nitrobenzyl chloride. The properties of the intermediate products in the synthesis and the final azo compound are given.

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## BIS( $\beta$ -CHLOROETHYL)-AMINES OF BICYCLIC COMPOUNDS

### III. SOME DERIVATIVES OF BENZOCYCLOHEPTANE WITH SUBSTITUENTS IN POSITION 7 OF THE BI-CYCLE

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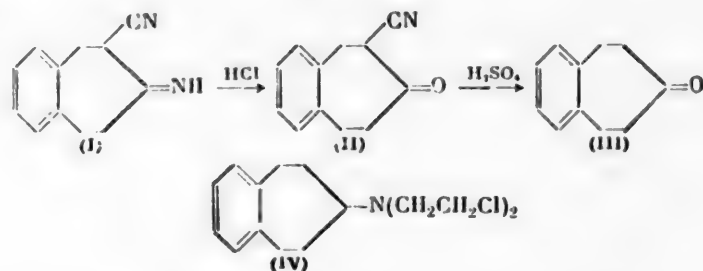
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In the present work we describe some 7-substituted derivatives of benzocycloheptane. The starting material was benzocycloheptan-7-one, which was obtained previously by heating 6-cyanobenzocycloheptan-7-one with sulfuric acid. In its turn, this was synthesized by cyclization of *o*-di-(cyanoethyl)-benzene by Ziegler's method [1].

We reproduced this scheme without complications except in the cyclization stage; as a result of the cyclization of *o*-di-(cyanoethyl)-benzene we isolated not 6-cyanobenzocycloheptan-7-one (II), but the intermediate compound, 6-cyanobenzocycloheptan-7-imine\* (I). 6-Cyanobenzocycloheptan-7-one was obtained by heating the imine with hydrochloric acid. 6-Cyanobenzocycloheptan-7-one was converted into benzocycloheptan-7-one (III) as described in the literature [1].



We were unable to find conditions for hydrolyzing the cyano group in compound (II) so as to isolate the corresponding  $\beta$ -ketocarboxylic acid or its ester.

From benzocycloheptan-7-one we prepared the oxime, which was reduced to the amine with lithium aluminum hydride; by the usual methods, the amine was converted to some of its derivatives, in particular 7-bis( $\beta$ -chloroethyl)-aminobenzocycloheptane (IV), which interested us in connection with our other work.

#### EXPERIMENTAL

**6-Cyanobenzocycloheptan-7-one (II).** A 5.51-g sample of 6-cyanobenzocycloheptan-7-imine (m. p. 139-140°) was boiled with 110 ml of a 6.5% aqueous solution of hydrochloric acid for 2 hr. The precipitate was collected and dried. It had m. p. 133-135° (from methanol). The yield was 4.88 g (88.3%). The product was insoluble in water and soluble in ether, alcohol, benzene, chloroform, and dichloroethane.

\* The cyclization and properties of the imine were reported in detail in separate article by A. K. Chizhov entitled "Preparation of 6-cyanobenzocycloheptan-7-imine" [2].

Found %: N 7.36, 7.59,  $C_{12}H_{11}ON$ . Calculated %: N 7.56.

Benzocycloheptan-7-one (III). A mixture of 9 g of 6-cyanobenzocycloheptan-7-one and 100 ml of 76.5% sulfuric acid was heated for 30 min on a boiling water bath. A reddish brown solution was formed as the cyano ketone dissolved. The ketone was steam distilled and collected from the cooled solution by filtration. The yield was 70.8% and the m. p. 38.5°. According to literature data [1]: yield 69% and m. p. 42-43°.

Benzocycloheptan-7-one oxime. To a solution of 5.35 g of benzocycloheptan-7-one in 30.2 ml of alcohol was added a saturated solution of sodium carbonate, and then a solution of 4.63 g of hydroxylamine hydrochloride in 9 ml of water was introduced dropwise over a period of 40 min with stirring. The reaction mixture obtained was stirred at room temperature for 5.5 hr and left overnight. The reaction product was collected, washed with water on the filter, and dried in a vacuum desiccator. The yield was 5.43 g (92.8%) and the m. p. 123-125°. The product was insoluble in water and readily soluble in alcohol, acetone, ethyl acetate, and benzene.

Found %: C 75.42; H 7.36; N 7.63,  $C_{11}H_{13}ON$ . Calculated %: C 75.50; H 7.48; N 7.90.

7-Aminobenzocycloheptane. A solution of 5.43 g of benzocycloheptan-7-one oxime in 112 ml of absolute ether was added dropwise with stirring over a period of 55 min to a suspension of 5.27 g of lithium aluminum hydride in 118 ml of absolute ether. The mixture obtained was boiled for 10.5 hr, 10 ml of water added dropwise over a period of 45 min with stirring, and then the mixture heated and stirred for a further 2 hr. The cooled reaction mixture was diluted with 20 ml of ether and filtered. The precipitate was washed with ether and chloroform. The ether-chloroform solution was dried with sodium sulfate, the solvent removed, and the residue vacuum distilled. The yield was 3.9 g (78.2%) and the b. p. 146° (20 mm). The product was readily soluble in alcohol, chloroform, and benzene, less soluble in ethyl acetate, and insoluble in water. It rapidly absorbed carbon dioxide in air.

Found %: C 81.69; H 9.62; N 8.49,  $C_{11}H_{15}N$ . Calculated %: C 81.93; H 9.38; N 8.68.

7-Aminobenzocycloheptane hydrochloride. An ether solution of 7-aminobenzocycloheptane was acidified with an ether solution of hydrogen chloride. The precipitate was recrystallized from anhydrous alcohol. It had m. p. 272-275°.

Found %: C 66.40; H 8.57; N 7.89; Cl 17.74,  $C_{11}H_{15}N \cdot HCl$ . Calculated %: C 66.86; H 8.11; N 7.09; Cl 17.94.

7-Acetaminobenzocycloheptane. A 0.36-g sample of 7-aminobenzocycloheptane was mixed with 2.23 ml of anhydrous alcohol and 0.105 ml of acetic anhydride. The reaction mixture was stirred for 1.5 hr and poured into 11 ml of water. The precipitate was collected, dried, and recrystallized from anhydrous ethyl acetate. The yield was 0.25 g (55.3%) and the m. p. 205-207°.

Found %: C 76.42, 76.85; H 8.15, 8.39; N 6.82,  $C_{13}H_{17}ON$ . Calculated %: C 76.80; H 8.44; N 6.89.

7-Bis( $\beta$ -hydroxyethyl)-aminobenzocycloheptane. A mixture of 1.33 g of benzocycloheptylamine and 0.73 g of ethylene oxide was heated for 9 hr in a sealed tube at 130-140°. The oily substance obtained was vacuum distilled and had b. p. 198-200° (0.2 mm),  $n_D^{20}$  1.5535. The yield was 1.5 g (73%).

Found %: C 72.10, 72.29; H 9.28, 9.37; N 5.51, 5.39,  $C_{15}H_{22}O_2N$ . Calculated %: C 72.30; H 9.24; N 5.62.

7-Bis( $\beta$ -chloroethyl)-aminobenzocycloheptane (IV). A mixture of 2.76 g of the hydroxy amine, 26.35 g of thionyl chloride, and 17 ml of anhydrous chloroform was boiled for 3 hr. The excess thionyl chloride and chloroform were removed in vacuum. To the residue was added 25 ml of 50% aqueous potassium carbonate and the mixture extracted with ether. The ether solution was dried with potassium carbonate, the ether removed, and the residue vacuum distilled. The yield was 1.97 g (62.2%) and the substance had b. p. 164-165° (0.1 mm),  $n_D^{20}$  1.5521.

Found %: C 62.59, 62.57; H 7.54, 7.40; N 4.63, 4.60,  $C_{15}H_{21}NCl_2$ . Calculated %: C 62.95; H 7.39; N 4.89.

7-Bis( $\beta$ -chloroethyl)-aminobenzocycloheptane hydrochloride. An ether solution of the amine (IV) was acidified with an ether solution of hydrogen chloride. The precipitate was collected, washed with ether, and dried in a vacuum desiccator over phosphorus pentoxide. The m. p. was 175-176°.

Found %: C 56.05; H 6.91; N 4.59; Cl 32.47, 32.57.  $C_{15}H_{11}NCl_2 \cdot HCl$ . Calculated %: C 55.80; H 6.87; N 4.34; Cl 33.00.

#### SUMMARY

Derivatives of benzocycloheptane with substituents in position 7 of the bi-cycle which have not been described in the literature were prepared.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation. A complete list of the cover-to-cover English translations appears at the back of this issue.*

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## CONVERSIONS OF CYCLOHEXANE ON A MOLYBDENUM CATALYST\*

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Among contemporary industrial processes for the aromatization of petroleum raw material a definite position is occupied by processes carried out on a molybdenum catalyst ( $\text{MoO}_3/\text{Al}_2\text{O}_3$ ) under a pressure of hydrogen [1]. Molybdenum catalysts have a high activity in the dehydrogenation of naphthenes [2-5]. Moreover, it has been established [6, 7] that under certain conditions under a pressure of hydrogen, 6-membered naphthenes are isomerized to 5-membered naphthenes on the same catalysts.

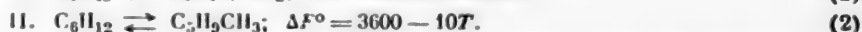
In the present work it was shown that when cyclohexane is passed over an aluminum-molybdenum catalyst ( $\text{MoO}_3/\text{Al}_2\text{O}_3$ ) under a hydrogen pressure of 10 to 40 atm and at temperatures of 445 to 495°, there are two parallel and reversible reactions, namely, dehydrogenation of the cyclohexane to benzene and isomerization of the cyclohexane to methylcyclopentane.

We undertook to study the effect of process conditions on the composition of the reaction products and to determine the factors by means of which the relative rates of dehydrogenation and isomerization of cyclohexane could be controlled.

It should be noted that the reaction was studied under conditions close to those adopted in industrial aromatization processes on the molybdenum catalyst.

To analyze the results, it was necessary to calculate the equilibrium ratios of the reacting substances accumulating as a result of the two reactions.

The free energies for these reactions could be calculated from the following approximate equations:



Equation (1) was taken from the work of Francis [8], and over the temperature range interesting us it agrees well with the experimental data of Frost and Zharkova [9, 10].

Equation (2) [11] also agrees well with experimental data [12].

On the basis of the equations presented the temperature dependences of the logarithms of the equilibrium constants  $K_I$  and  $K_{II}$  for reactions I and II, respectively, may be expressed in the following way:

$$\lg K_I = -\frac{53700}{4.573T} + 21.12, \quad (3)$$

$$\lg K_{II} = -\frac{3600}{4.573T} + 2.19. \quad (4)$$

\* Presented at the All-Union Conference on Organic Catalysis on November 18, 1959, in Moscow.

where  $K_I = \frac{P_2 \cdot P_4^3}{P_1}$ ;  $K_{II} = \frac{P_3}{P_1}$ ;  $P_1, P_2, P_3, P_4$  are the partial pressures of cyclohexane, benzene, methylcyclopentane, and hydrogen, respectively.

The equilibrium constants  $K_I$  and  $K_{II}$  for the temperatures at which the experiments were carried out are given below:

Temperature . . . . .	455°	460	475	495
$K_I$ . . . . .	$8.7 \cdot 10^4$	$12.6 \cdot 10^4$	$25.7 \cdot 10^4$	$63.1 \cdot 10^4$
$K_{II}$ . . . . .	12.88	13.06	13.74	14.64

On the basis of these values of  $K_I$  and  $K_{II}$ , we calculated the percentage content of benzene, methylcyclopentane, and cyclohexane in the equilibrium mixture in relation to the experimental conditions used. The results of the calculations are given in Tables 1 and 2. The data in the latter make it possible to compare the equilibrium composition of the reaction products with that found experimentally.

The essential conclusion from the comparison of these data is that we studied the dehydrogenation of cyclohexane under conditions where the benzene concentration in the mixture of the reagents was far from the equilibrium value.

#### Working Procedure and Starting Materials

The experiments were carried out on a flow apparatus designed for operation at an elevated pressure; the apparatus and working procedure were described previously [7].

For the experiments we used a molybdenum catalyst which contained 10% of  $\text{MoO}_3$  and 90% of  $\text{Al}_2\text{O}_3$ . The catalyst charge in the reactor was 50 ml.

Cyclohexane with b. p.  $80.8^\circ$  (750 mm),  $d_4^{20}$  0.7784,  $n_D^{20}$  1.4262 [13] was prepared by hydrogenation of benzene over a nickel catalyst.

The reaction products were a complex mixture of hydrocarbons, consisting of cyclohexane, benzene, methylcyclopentane, and small amounts of paraffins and unsaturated hydrocarbons.

The unsaturated hydrocarbon content of the catalyzates was determined from the bromine number by Francis's method [14]. The amount of benzene was determined by a dispersion method [15] with a Pulfrich refractometer.

For determination of the cyclohexane content, after removal of the unsaturated and aromatic hydrocarbons by treatment with 98% sulfuric acid, the catalyzates were dehydrogenated by Zelinski's method over palladized charcoal (30% Pd) at  $320^\circ$  in the absence of hydrogen supplied from outside [16]. The product was passed over the catalyst several times until a constant refractive index was reached. The benzene content was determined by the dispersion method [15] and the cyclohexane content of the catalyzate calculated.

The benzene was removed from the dehydrogenation product by treatment with concentrated sulfuric acid. The aniline point of the remaining hydrocarbon was determined and used to calculate the methylcyclopentane and hexane content of the product [17].

In most cases, the degree of isomerization of cyclohexane to methylcyclopentane was characterized by the total content of methylcyclopentane and hexanes in the catalyzate.

The latter was possible as the content of hexanes normally did not exceed a few percent. In addition, according to literature data, methylcyclopentane is the intermediate product in the formation of hexanes during the destructive hydrogenation of cyclohexane on a molybdenum catalyst [18].

#### Effect of Temperature and Cyclohexane Input Rate on the Reaction Product Composition

To study this problem we carried out experiments with various cyclohexane inputs at temperatures of 455, 475, and  $495^\circ$ . The experiments were carried out at a pressure of 20.4 atm and approximately the same molar ratio of hydrogen and cyclohexane ( $M_H:M_C$ ), which was close to 10 (Fig. 1, Table 1).

TABLE 1

Effect of Temperature and Cyclohexane Input Rate on the Reaction Product Composition:  
Working pressure 20.4 atm, molybdenum catalyst (sample A)

Experiment No.	Experimental conditions			Contents of equilibrium mixture* (weight %)			Catalyzate composition (weight %)				
	cyclohexane input per hr		molar ratio of hydrogen to cyclohexane	benzene	methylcyclopentane	cyclohexane	benzene	methylcyclopentane	cyclohexane	hexane	unsaturateds
	ml	ratio of cyclohexane and catalyst volumes, liter/liter									
At 455°											
99	80	1.6	10.2	46.8	49.3	3.9	8.9	12.9**	77.6	--	0.6
98	40	0.8	9.5				14.1	23.8	60.1	1.4	0.6
100	20	0.4	9.4	46.8	49.3	3.9	21.7	25.8	49.5	2.6	0.4
At 475°											
96	160	3.2	10.4	70.8	27.1	2.1	10.0	12.6	74.5	2.2	0.7
95	80	1.6	10.2	70.8	27.1	2.1	10.4	—	—	—	0.7
94	40	0.8	9.3	70.8	27.1	2.1	31.8	—	—	—	0.7
97	20	0.4	9.2	70.8	27.1	2.1	35.7	—	—	—	0.4
At 495°											
93	160	3.2	10.2	84.6	14.4	1.0	17.8	23.3	55.3	2.7	0.9
92	80	1.6	9.8	84.6	14.4	1.0	31.5	31.4	32.8	3.1	1.2
90	40	0.8	8.8	84.6	14.4	1.0	44.8	34.6	13.9	6.0	0.7
91	20	0.4	8.6	84.6	14.4	1.0	55.2	29.8	6.6	7.9	0.5

\* The calculation was carried out for a pressure of 20.4 atm and a molar ratio of hydrogen: cyclohexane = 10.2.

\*\* Total content of methylcyclopentane and hexanes.

At a moderate degree of cyclohexane conversion, not exceeding 50-60%, the methylcyclopentane content of the catalyzates exceeded the benzene content, which indicated that under the conditions used the cyclohexane isomerization rate was greater than the dehydrogenation rate.

Further analysis of the data obtained showed that as the degree of cyclohexane conversion increased there was a clear tendency for the methylcyclopentane: benzene ratio to decrease. This was observed particularly clearly at a reaction temperature of 495°.

This change in the composition of the reaction products was caused by the fact that as the cyclohexane input decreased, and consequently the degree of its conversion increased, there was a continuous increase in the benzene content of the catalyzate, which, however, did not reach the equilibrium concentration. As regards methylcyclopentane, at 495° the curve of its content in the catalyzate showed a maximum which was preceded by sharp retardation of the formation of this hydrocarbon (Fig. 1).

This result may be explained if it is assumed that under the conditions used (495° and a hydrogen pressure of 19 atm) the equilibrium of cyclohexane isomerization is displaced toward methylcyclopentane and that of cyclohexane dehydrogenation is displaced toward benzene. Under these conditions, the relative concentrations of methylcyclopentane and benzene in the reaction products must be determined primarily by the ratio of the cyclohexane dehydrogenation and isomerization rates. Due to the high rate of isomerization, an increase in the degree of cyclohexane conversion first led to the predominant accumulation of methylcyclopentane in the catalyzate, and the maximum content of this reached 34.6%.

On the other hand, the equilibrium state for the methylcyclopentane-cyclohexane-benzene-hydrogen system under the given conditions is such that the benzene concentration of the equilibrium mixture of



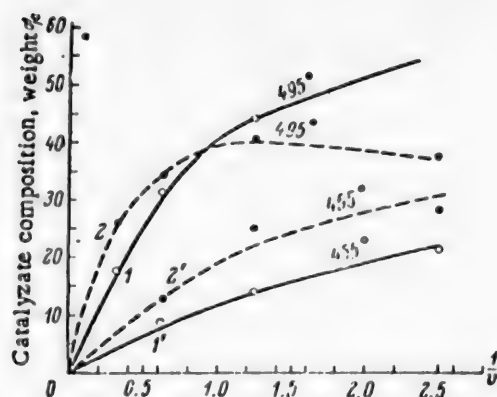


Fig. 1. Effect of cyclohexane input space velocity (in liters of cyclohexane passed through a liter of catalyst per hr) on the concentration of the reaction products at a pressure of 20.4 atm and a molar ratio of hydrogen: cyclohexane = 10.2; 1 and 1') benzene; 2 and 2') methylcyclopentane + hexanes.

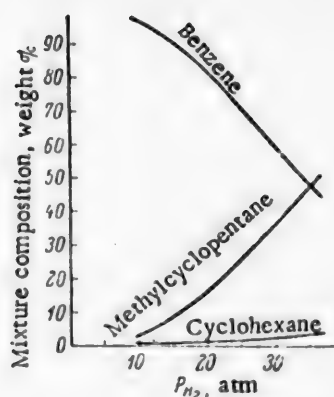


Fig. 2. Ratio of cyclohexane, methylcyclopentane, and benzene in an equilibrium mixture in relation to the partial hydrogen pressure at 495° and a molar ratio of hydrogen: cyclohexane = 10.2. P<sub>H<sub>2</sub></sub> is the partial hydrogen pressure (atm).

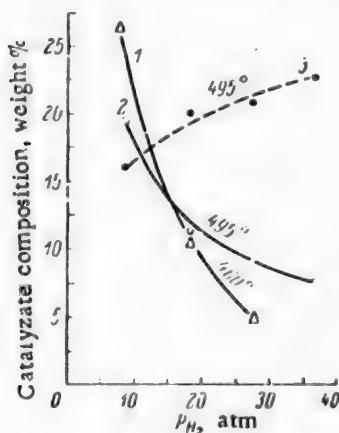


Fig. 3. Effect of partial hydrogen pressure on reaction product composition. P<sub>H<sub>2</sub></sub> = partial hydrogen pressure (atm); 1 and 2) benzene; 3) methylcyclopentane + hexanes.

hydrocarbons is approximately 85%. Therefore, with a further increase in the cyclohexane conversion the methylcyclopentane content of the catalyzate inevitably fell, and this produced the maximum on the curve for this hydrocarbon illustrated in Fig. 1.

#### Effect of Partial Hydrogen Pressure

One of the parameters of the process which might be used for controlling the ratio of the cyclohexane isomerization and dehydrogenation rates and thus changing the ratio of methylcyclopentane and benzene in the reaction products is the hydrogen pressure.

This conclusion can be drawn from an examination of the ratios of cyclohexane, methylcyclopentane, and benzene which accumulate under equilibrium conditions at 495° in relation to the hydrogen pressure. Thus, with an increase in the partial hydrogen pressure (Fig. 2, Table 2) the amount of benzene in the equilibrium mixture of hydrocarbons falls sharply; the opposite is observed for methylcyclopentane, and the amount of it increases considerably.

We found similar relations on studying the conversions of cyclohexane on a molybdenum catalyst under conditions at which the benzene concentration in the reacting mixture of hydrocarbons was quite far from the equilibrium value (Table 2).

The effect of the hydrogen pressure was studied at two temperatures, 460 and 495°. In each series of experiments the partial pressure of the hydrocarbon was kept approximately constant and was ~2 atm.

The partial hydrogen pressure was varied over the range 7.8 to 36.8 atm.

An examination of the experimental results (Fig. 3 and Table 2) leads to the conclusion that the benzene content of the catalyzates decreased considerably with an increase in the partial hydrogen pressure. This was observed at reaction temperatures of both 495° and 460°.

TABLE 2

Effect of Partial Hydrogen Pressure on Reaction Product Composition. Molybdenum catalyst (sample B)

Experiment No.	Experimental conditions				Contents of equilibrium mixture (weight %)			Catalyzate composition (weight %)				
	partial pressure (atm)		cyclohexane input per hr	molar ratio of hydrogen: cyclohexane	benzene	methylcyclopentane	cyclohexane	benzene	methylcyclopentane	cyclohexane	hexanes	unsaturated compounds
	hydrogen	cyclohexane										
At 460°												
107	27.7	1.9	20	14.4	27.9	67.0	5.1	5.0	—	—	—	0.6
105	18.4	2.0	20	9.3	50.0	46.4	3.6	11.3	—	—	—	0.6
106	7.8	1.9	20	4.1	92.5	7.0	0.5	27.9	—	—	—	1.4
At 495°												
101	36.8	1.9	80	19.0	93.0	53.4	3.6	7.9	24.9	65.4	1.1	1.0
102	27.6	2.0	80	14.0	64.0	33.7	2.3	8.7	22.1*	68.0	—	1.2
103	18.4	2.0	80	8.0	84.3	14.2	1.0	12.9	18.3	65.1	1.9	1.8
104	8.9	2.2	80	4.1	96.8	2.2	1.0	19.2	16.5	61.1	0.9	2.5

\* Total content of methylcyclopentane and hexanes.

Thus, the dehydrogenation of cyclohexane on a molybdenum catalyst is retarded by hydrogen.

An increase in the hydrogen pressure had a completely different effect on the rate of the other, parallel reaction, namely the isomerization of cyclohexane to methylcyclopentane. In this case an increase in the hydrogen pressure led to an increase in the amount of methylcyclopentane in the catalyzate (Fig. 3).

Thus, by changing the hydrogen pressure it is possible to regulate the relative rates of cyclohexane dehydrogenation and isomerization and thus change the ratio of methylcyclopentane and benzene in the reaction products.

This relation may be explained if it is assumed that dehydrogenation and isomerization of cyclohexane occur on different active centers of the molybdenum catalyst. By retarding dehydrogenation, an increase in the hydrogen pressure leads to an increase in the cyclohexane concentration in the mixture of reacting substances. Due to this there is an increase in the rate of isomerization, which occurs on other active centers.

We would like to thank A. A. Vvedenskii for advice on the thermodynamic calculations.

#### SUMMARY

1. The conversions of cyclohexane on a molybdenum catalyst ( $\text{MoO}_3/\text{Al}_2\text{O}_3$ ) at 455–495°, a hydrogen pressure of 10–39 atm, and various ratios of hydrogen and hydrocarbon were studied.
2. It was shown that under these conditions two parallel and reversible reactions occur on the catalyst, namely, dehydrogenation of cyclohexane to benzene and isomerization of cyclohexane to methylcyclopentane.
3. The rates of cyclohexane isomerization and dehydrogenation are commensurate at 455–495° and a hydrogen pressure of about 20 atm.
4. The quantitative ratio of benzene and methylcyclopentane in the catalyzate changes as the degree of cyclohexane conversion increases.
5. The rate of benzene formation decreases and the rate of methylcyclopentane formation increases as the hydrogen pressure increases.

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## SYNTHESIS OF CHELANTS AMONG AZOXY COMPOUNDS

### II. NEW SYNTHESIS OF 2-(2'-AMINOPHENYLAZOXY)-4-METHYLPHENOL AND THE SYNTHESIS OF 2-(2'-BROMOPHENYLAZOXY)-4-METHYLPHENOL

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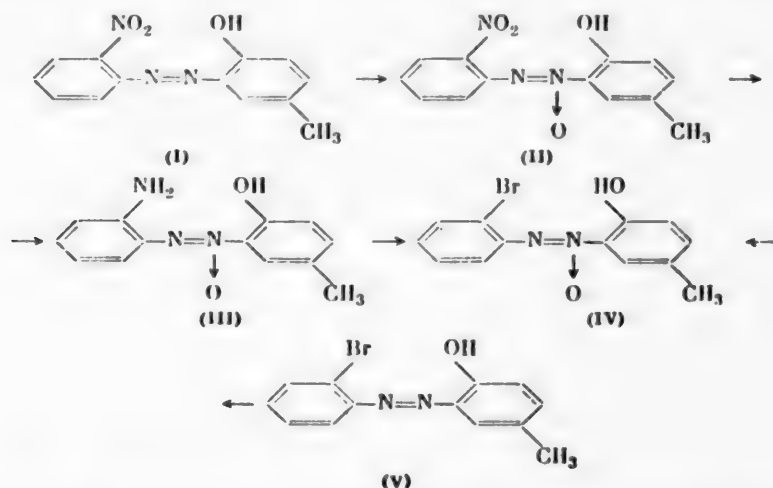
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 11, pp. 3708-3711,

November, 1960

Original article submitted January 1, 1960

The synthesis of 2-(2'-aminophenylazoxy)-4-methylphenol\* (III) by hydrazinolysis of 2-(2'-phthaloylamino-phenylazoxy)-4-methylphenol was reported previously [1]. In view of the results of catalytic reduction of 2-nitrophenylazoxybenzene to 2-aminophenylazoxybenzene [3, 4], we decided to apply this method to the azoxy compounds which could be obtained by oxidation of 2-nitro-2'-hydroxy-5'-methylazobenzene (I).

In the oxidation of 2-nitro-2'-hydroxy-5'-methylazobenzene (I) with peracetic acid, we isolated only one azoxy compound (II), which was reduced with hydrogen in the presence of platinum oxide to give the corresponding amine, which was found to be identical with 2-(2'-aminophenylazoxy)-4-methylphenol (III).



For a more accurate determination of the structure, substance (III) was converted into 2-(2'-bromophenylazoxy)-4-methylphenol (IV) by the Sandmeyer reaction, and (IV) was found to be identical with the oxidation product of 2-bromo-2'-hydroxy-5'-methylazobenzene (V). Neither of the products were brominated with the stoichiometric amount of bromine under mild conditions, and this further confirms the accuracy of the structures proposed, in which the oxygen of the azoxy group is attached to the nitrogen in the position ortho to the hydroxyl.

\* Nomenclature according to new work [2]; this compound was previously [1] called the *B*-isomer of 2-amino-2'-hydroxy-5'-methylazoxybenzene.

## EXPERIMENTAL

2-Nitro-2'-hydroxy-5'-methylazobenzene (I) was synthesized by azo coupling of diazotized o-nitroaniline with p-cresol in a sodium carbonate-alcohol medium. The product was purified by reprecipitation from chloroform with ligroin. It had m. p. 108-110°; literature data [6]: m. p. 107-108°.

Found %: C 60.61; 60.86; H 4.42, 4.47.  $C_{13}H_{11}O_3N_3$ . Calculated %: C 60.70; H 4.20.

2-(2'-Nitrophenylazoxy)-4-methylphenol (II). To a solution of 3.2 g of 2-nitro-2'-hydroxy-5'-methylazobenzene in 150 ml of glacial acetic acid was added 40 ml of 30% hydrogen peroxide and the mixture heated at 65-75° for 18 hr. The color of the solution gradually changed from dark red to orange. After filtration, the solution was poured onto 400 g of ice. The product liberated was washed on the filter with distilled water until it was no longer acid to Congo, dried on the filter, dissolved in 100 ml of methanol, precipitated with 30 ml of water, and dried in a vacuum desiccator over calcium chloride and phosphorus pentoxide. The yield was 1.0 g (30%). The yellow powder had m. p. 102-103°. It was readily soluble in methanol, ethanol, chloroform, benzene, ether, and other organic solvents. It was difficultly soluble in water.

Found %: C 57.01, 57.24; H 4.43, 4.36.  $C_{13}H_{11}O_4N_3$ . Calculated %: C 57.10; H 4.00.

2-(2'-Aminophenylazoxy)-4-methylphenol (III). A suspension of 0.2 g of platinum oxide in 20 ml of ether was reduced in a stream of hydrogen, a solution of 0.4 g of 2-(2'-nitrophenylazoxy)-4-methylphenol in 100 ml of ether added, and shaking with hydrogen at room temperature continued until the absorption of hydrogen ceased (~1.5-2 hr). The solution was filtered to remove the catalyst and saturated with dry hydrogen chloride. The precipitate was washed with ether, dissolved in water, and neutralized with sodium bicarbonate. The amine (III) liberated was recrystallized from dilute alcohol (1:2) (30 ml) and dried in a vacuum desiccator over calcium chloride and phosphorus pentoxide. The yield was 0.04 g (11%) and the m. p. 125.5°. The melting point of the amine obtained by hydrazinolysis was 126° [1]. The melting point of a mixture was 125.5°.

Found %: C 63.95, 64.0; H 5.62, 5.69; N 17.36, 17.50.  $C_{13}H_{13}O_2N_3$ . Calculated %: C 64.19; H 5.35; N 17.28.

2-(2'-Bromophenylazoxy)-4-methylphenol (IV). a) From 2-(2'-aminophenylazoxy)-4-methylphenol (III). A solution of sodium nitrite (0.25 g in 10 ml of water) was added to a mixture of 0.8 g of 2-(2'-aminophenylazoxy)-4-methylphenol and 62.5 ml of 45% hydrobromic acid stirred at 0-2°. For the preparation of cuprous bromide, a mixture of 1.1 g of copper sulfate, 0.32 g of copper turnings, 2.4 g of sodium bromide, 0.32 ml of concentrated sulfuric acid, and 16 ml of water was heated under reflux for 4 hr, and then ~0.5 g of sodium sulfite was added. The solution of the diazonium salt was added slowly with stirring to the solution of cuprous bromide at 20-25°. The reaction mixture was stirred for 2-3 hr and the precipitate collected, washed with water (~50 ml), and recrystallized successively twice from aqueous (1:1) acetone (90 ml and 20 ml) and twice from dilute (1:1) alcohol (28 and 16 ml). The yield was 0.03 g (3%) and the m. p. 95.5-96°. The melting point of a mixture with 2-(2'-bromophenylazoxy)-4-methylphenol obtained by oxidation of the corresponding azo compound was 95.5-96°.

Found %: C 51.02, 51.20; H 3.91, 3.98; N 9.02, 8.98.  $C_{13}H_{11}O_2N_2Br$ . Calculated %: C 50.81; H 3.58; N 9.12.

b) From 2-bromo-2'-hydroxy-5'-methylazobenzene (V). 2-Bromo-2'-hydroxy-5'-methylazobenzene [6] was purified by successive recrystallizations from acetic acid and methanol. The m. p. was 114°. Literature data [4]: m. p. 116°. The acetyl derivative had m. p. 85-86°. Literature data [4]: m. p. 85°.

To a solution of 1.4 g of the azo compound (V) in glacial acetic acid (100 ml) was added 16.7 ml of 30% hydrogen peroxide and the mixture heated at 70-80° for 18 hr. The product was isolated analogously to 2-(2'-nitrophenylazoxy)-4-methylphenol (II). The product was dried on the filter and recrystallized from 40 ml of a mixture of acetone and water (3:1). We obtained 0.2 g (15%) of the substance with m. p. 96°. It formed yellow scales. It was readily soluble in ethanol, methanol, chloroform, benzene, acetone, and other organic solvents and difficultly soluble in water. Bromination of substance (IV) yielded only the starting material (mixed melting point 96°).

## SUMMARY

2-(2'-Nitrophenylazoxy)-4-methylphenol, 2-(2'-aminophenylazoxy)-4-methylphenol, and 2-(2'-bromophenylazoxy)-4-methylphenol were synthesized.

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# SYNTHESIS OF SUBSTITUTED ACIDS THROUGH FURAN DERIVATIVES

## IV. PREPARATION OF $\gamma$ -AMINO ACIDS

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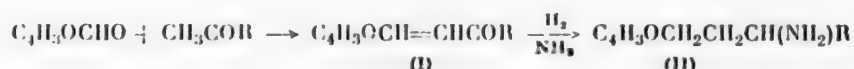
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November, 1960

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The preparation of  $\alpha$ -amino acids (as benzoyl derivatives) from the corresponding amino derivatives of furans and also ethyl ethers of  $\alpha$ -hydroxy acids from the corresponding furylcarbinols was described in previous work [1]. In the present communication, we describe the synthesis of  $\gamma$ -amino acids by oxidation of benzoyl derivatives of furan amines.



The preparation of unsaturated ketones (I) by condensation of furfural with ketones has been described in detail in the literature. The amines (II) were obtained quite readily by reductive amination of the unsaturated ketones. Thus, the reduction of a series of  $\alpha$ ,  $\beta$ -unsaturated ketones of the furan series over Raney nickel at a pressure of 120 atm and 150° to form saturated amines in yields of 50-70% has been described [2].

We studied the reductive amination of four unsaturated carbonyl compounds of the furan series  $\text{C}_4\text{H}_5\text{OCH}=\text{CHCOR}$  ( $\text{R} = \text{H}, \text{CH}_3, \text{C}_6\text{H}_5, \text{C}_4\text{H}_5\text{O}$ ). In determining the optimal hydrogenation conditions, we found that the best yield of amine was obtained when the reaction was carried out in alcohol saturated with ammonia in the presence of Raney nickel at an initial pressure of 85 atm and 110°.

Together with amines, we also obtained a saturated ketone and when  $\text{R} = \text{C}_6\text{H}_5$ , only the saturated ketone was isolated (Table 1).

TABLE 1

R in $\text{C}_4\text{H}_5\text{OCH}=\text{CHCOR}$	Yield (%)	
	$\text{C}_4\text{H}_5\text{OCH}_2\text{CH}_2\text{COR}$	$\text{C}_4\text{H}_5\text{OCH}_2\text{CH}_2\text{CH}(\text{NH}_2)\text{R}$
H	23	30
$\text{CH}_3$	51	44
$\text{C}_6\text{H}_5$	72	—
$\text{C}_4\text{H}_5\text{O}$	50	35

To characterize the amines obtained, we plotted their ultraviolet spectra\* and compared them with the ultraviolet spectrum of 1-amino-1-( $\alpha$ -furyl)-ethane, which was obtained by reduction of acetylfuran oxime with zinc dust; the band at 260-270 m $\mu$  is characteristic of the furan nucleus (figure).

\* The ultraviolet spectra were plotted with an SF-4 spectrophotometer.



Absorption spectra of amines (II). 1) 1-Amino-1,3-di-( $\alpha$ -furyl)-propane; 2) 1-amino-1-( $\alpha$ -furyl)-ethane; 3) 3-amino-3-( $\alpha$ -furyl)-propane; 4) 2-amino-4-( $\alpha$ -furyl)-butane.

TABLE 2

Amine	pH
$C_6H_5OCH_2CH_2CH(NH_2)C_6H_5O$	8,60
$C_6H_5OCH(NH_2)CH_3$	8,80
$C_6H_5OCH_2CH_2CH_2NH_2$	8,88
$C_6H_5OCH_2CH_2CH(NH_2)CH_3$	9,09

We also measured the pH of propanol solutions of the amines we obtained\* (Table 2).

It is readily seen that the basicity of these amines increases in the distance of the amino group from the furan nucleus.

The benzoyl derivatives of the amines were then oxidized with potassium permanganate to the benzoyl  $\gamma$ -amino acids; the latter were difficult to purify due to difficulties in recrystallization.

## EXPERIMENTAL

### Unsaturated Ketones (I)

**Furfurylideneacetone.** To an aqueous methanol solution of 1,5 moles of furfural and 3,4 moles of acetone was added 30 ml of 30% sodium hydroxide solution dropwise at a temperature of no higher than 10°;

after 4 hr, the mixture was neutralized with sulfuric acid. The yield was 70%, the b. p. 109-110° (9 mm), and the m. p. 36-37° [3].

**Furfurylideneacetyl furan** was prepared analogously. The yield was 84% and the m. p. 88-89° (from methanol) [4].

**Furfurylideneacetophenone.** A solution of 5 g of sodium in 70 ml of anhydrous methanol was added dropwise to a solution of 0.2 mole of acetophenone and 0.2 mole of furfural in 50 ml of anhydrous methanol at 0°. After 3 hr, the mixture was poured into water and neutralized with acetic acid. The yield was 70% and the b. p. 184-185° (10 mm) [5].

**Furylacrolein.** To a solution of 7 g of sodium hydroxide in 1400 ml of water at 0° was added 1 mole of furfural and then a solution of 1,3 moles of acetaldehyde in 300 ml of water. After 2 hr, the organic layer was washed with water, dried with  $CaCl_2$ , and distilled. The yield was 80%, the m. p. 49-50°, and the b. p. 105-110° (12 mm) [6].

**Reductive amination of unsaturated ketones of the furan series.** To a solution of 0.1 mole of ketone in 30 ml of anhydrous alcohol saturated with ammonia was added 3 g of Raney nickel and the mixture hydrogenated in a 0,25-liter rotating autoclave at 110° and an initial hydrogen pressure of 85 atm. When the pressure had fallen to 63 atm, the autoclave was cooled and the catalyst removed by filtration. The filtrate was acidified with acetic acid, the alcohol removed by distillation, the saturated ketone extracted with ether, and the extract dried with magnesium sulfate. After removal of the solvent, the ketone was vacuum distilled. The aqueous layer was made alkaline, the amine extracted with ether, and the extract dried with alkali. After removal of the solvent, the amine was vacuum distilled. The benzoyl derivatives of the amines were obtained by the usual method, namely the action of benzoyl chloride in a strongly alkaline medium.

1. From 13,6 of furfurylideneacetone we obtained **furfurylaceton** in a yield of 7 g (51%).

B. p. 98-100° (20 mm),  $n_D^{20}$  1,4712,  $d_4^{20}$  1,0293; literature data [7]: b. p. 95° (15 mm),  $n_D^{20}$  1,4697,  $d_4^{20}$  1,0258.

\* The pH values of the solutions were measured with an LP-5 instrument with a glass electrode at 19°.

2-Amino-4- $\alpha$ -furylbutane: yield 6 g (44 %).

B. p. 85-93° (20 mm),  $n_D^{20}$  1.4732,  $d_4^{20}$  0.9488,  $M_{RD}$  41.17; calc. 41.05; literature data [7]: b. p. 102° (15 mm),  $n_D^{20}$  1.4730.

Benzoyl derivative: m. p. 109-110° (from ligroin).

Found %: C 74.12, 74.19; H 7.21, 7.18; N 5.52, 5.31.  $C_{15}H_{17}O_2N$ . Calculated %: C 74.05; H 7.04; N 5.76.

2. From 12.2 g of furalacrolein we obtained 3- $\alpha$ -furylpropanal in a yield of 2.8 g (23%).

B. p. 71-73° (10 mm),  $n_D^{20}$  1.4757, literature data [8]: b. p. 31-82° (17 mm),  $n_D^{20}$  1.4766.

1-Amino-3- $\alpha$ -furylpropane: yield 3.6 g (30%).

B. p. 70-71° (20 mm),  $n_D^{20}$  1.4852,  $d_4^{20}$  1.001,  $M_{RD}$  35.83; calc. 36.45; literature data [9]: b. p. 172-173° (754 mm).

Benzoyl derivative: m. p. 59-60° (from ligroin).

Found %: C 73.28, 73.42; H 6.72, 6.70.  $C_{14}H_{15}O_2N$ . Calculated %: C 73.34; H 6.59.

3. From 9.4 g of furfurylideneacetyl furan we obtained the following substances by hydrogenation in 150 ml of ethanol at an initial pressure of 40 atm.

Furfurylacetyl furan: yield 4.2 g (50%).

B. p. 147-148° (13 mm),  $n_D^{20}$  1.5225,  $d_4^{20}$  1.1442.

1-Amino-1,3-di-( $\alpha$ -furyl)-propane: yield 3.5 g (35%).

B. p. 140-141° (14 mm),  $n_D^{20}$  1.5012,  $d_4^{20}$  1.0701,  $M_{RD}$  52.67; calc. 53.79.

Benzoyl derivative: m. p. 109-110° (from ligroin).

Found %: N 5.22, 5.33.  $C_{18}H_{17}O_3N$ . Calculated %: N 4.74.

Benzoyl derivatives of  $\gamma$ -amino acids. To a solution of 0.01 mole of the benzoyl derivative of the amine in 100 ml of anhydrous acetone were added 1 ml of 20% potassium hydroxide solution and 1 ml of alcohol, and then a solution of 8.2 g of potassium permanganate in 250 ml of water was introduced with stirring at a temperature no higher than 15°. When the solution had been decolorized, 8.3 g of finely ground potassium permanganate was added and the mixture left overnight. The manganese dioxide was removed by filtration and washed with hot water. The combined filtrates were evaporated to dryness and the residue dissolved in 25 ml of water and boiled with charcoal. Hydrogen chloride was passed into the filtrate. The benzoyl derivatives of the  $\gamma$ -amino acids crystallized after a long time with strong cooling.

N-Benzoyl- $\gamma$ -aminobutyric acid: yield 50%, m. p. 81°.

Found %: C 63.70, 63.81; H 6.52, 6.45.  $C_{11}H_{13}O_3N$ . Calculated %: C 63.75; H 6.32.

N-Benzoyl- $\gamma$ -aminovaleric acid: yield 65%, m. p. 132-133° [10].

Found %: C 65.34, 65.36; H 6.84, 6.89.  $C_{12}H_{15}O_3N$ . Calculated %: C 65.14; H 6.83.

#### SUMMARY

The reductive amination of  $\alpha$ ,  $\beta$ -unsaturated ketones of the furan series under pressure was studied. On the example of  $\gamma$ -aminobutyric and  $\gamma$ -aminovaleric acids, it was shown that benzoyl derivatives of  $\gamma$ -amino acids may be synthesized by oxidation of benzoyl derivatives of amines obtained by reductive amination of furfurylidene ketones.

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MECHANISM OF THE CONVERSION OF  $\alpha$ -ACYLAMINO-  
 $\beta$ -HYDROXYPROPIOPHENONES INTO THE  
CORRESPONDING BENZOYLACETYL

II. SYNTHESIS AND CLEAVAGE OF  $\alpha$ -BENZENESULFONAMIDEOACRYLOPHENONES

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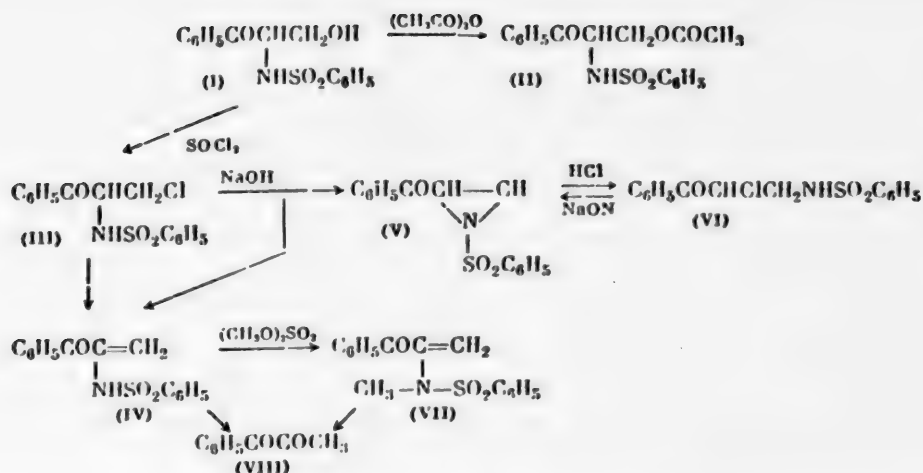
In a previous communication [1], we put forward the hypothesis that the conversion of  $\alpha$ -benzenesulfonamido- $\beta$ -hydroxypropiophenones into the corresponding benzoylacetyls proceeds through the formation of  $\alpha$ -benzenesulfonamidoacrylophenones. We were unable to isolate these hypothetical intermediate compounds directly from the reaction mixture, evidently due to the fact that under the conditions of the reaction studied their decomposition rate exceeded their rate of formation from the corresponding  $\alpha$ -benzenesulfonamido- $\beta$ -hydroxypropiophenones. In order to check the hypotheses, we undertook the synthesis of  $\alpha$ -benzenesulfonamido- and  $\alpha$ -benzenesulfonylmethylamidoacrylophenones.

Attempts at the direct conversion of  $\alpha$ -benzenesulfonamido- $\beta$ -hydroxypropiophenone (I) and  $\alpha$ -benzenesulfonylmethylamido- $\beta$ -hydroxypropiophenone (Ia) into the corresponding acrylophenones in analogy with the preparation of p-nitro- $\alpha$ -acetylaminocacrylophenone [2, 3] were unsuccessful; both compounds were recovered when boiled with pyridine; when heated with acetic anhydride,  $\alpha$ -benzenesulfonylmethylamido- $\beta$ -hydroxypropiophenone (Ia) did not react, while  $\alpha$ -benzenesulfonamido- $\beta$ -hydroxypropiophenone (I) was converted into  $\alpha$ -benzenesulfonamido- $\beta$ -acetoxypopiophenone (II).

Treatment of  $\alpha$ -benzenesulfonamido- $\beta$ -hydroxypropiophenone (I) with thionyl chloride in the presence of pyridine yielded  $\alpha$ -benzenesulfonamido- $\beta$ -chloropropiophenone (III). When heated with a tertiary amine (pyridine and triethylamine), this compound readily lost a molecule of hydrogen chloride and was converted into  $\alpha$ -benzenesulfonamidoacrylophenone (IV), and when treated with caustic alkalis in an aqueous medium it formed a mixture of 62.4% of 1-benzenesulfonyl-2-benzoylaziridine (V) and 37.6% of the acrylophenone (IV). Analogous results were obtained by treatment of  $\alpha$ -benzenesulfonamido- $\beta$ -chloropropiophenone (III) with sodium ethylate in alcohol.

When 1-benzenesulfonyl-2-benzoylaziridine (V) was heated with an aqueous alcohol solution of hydrochloric acid, the three-membered ring was opened to form  $\alpha$ -chloro- $\beta$ -benzenesulfonamidopropiophenone (VI), which remained unchanged when heated with pyridine, but was reconverted into compound (V) by the action of caustic alkalis.\* Methylation of  $\alpha$ -benzenesulfonamidoacrylophenone (IV) with dimethyl sulfate in an aqueous medium in the presence of sodium hydroxide yielded  $\alpha$ -benzenesulfonylmethylamidoacrylophenone (VII).

\* Analogous conversions occur with 1-(p-toluenesulfonamido)-2-bromoethylbenzene [4].



Experiments on the hydrolysis of benzenesulfonamido- and benzenesulfonylmethylamidoacrylophenones (IV) and (VII) with mineral acids showed that when boiled with 1-2% aqueous alcohol solutions of sulfuric acid for 30-60 min, both of these compounds decomposed completely to benzoylacetyl (VIII) and the corresponding sulfonamide. When heated under the same conditions,  $\alpha$ -benzenesulfonamido- and  $\alpha$ -benzenesulfonylmethylamido- $\beta$ -hydroxypropiofenones (I) and (II) did not change and could be recovered quantitatively from the reaction mixture.

Thus, we showed that when heated with mineral acids,  $\alpha$ -benzenesulfonamidoacrylophenones are cleaved quantitatively with the formation of benzoylacetyl and the corresponding sulfonamide, and the rate of this cleavage is much greater than the rate of cleavage of the corresponding sulfonamidohydroxypropiofenones.

## EXPERIMENTAL

$\alpha$ -Benzenesulfonamido- $\beta$ -acetoxypropiofenone (II). A mixture of 6.1 g of  $\alpha$ -benzenesulfonamido- $\beta$ -hydroxypropiofenone and 15 ml of acetic anhydride was heated on a boiling water bath for 4 hr and then poured into water. An oil separated and this crystallized rapidly. The precipitate was collected, washed with water, dried, and recrystallized from alcohol. We obtained 5.4 g (77.8%) of  $\alpha$ -benzenesulfonamido- $\beta$ -acetoxypropiofenone as a colorless, crystalline substance with m. p. 92-92.5°.

Found %: C 58.67; H 4.83; N 4.05.  $\text{C}_{17}\text{H}_{17}\text{O}_5\text{NS}$ . Calculated %: C 58.77; H 4.93; N 4.03.

$\alpha$ -Benzenesulfonamido- $\beta$ -chloropropiofenone (III). Into a flask with a stirrer, thermometer, and reflux condenser with a calcium chloride tube were placed 6.1 g of  $\alpha$ -benzenesulfonamido- $\beta$ -hydroxypropiofenone, 30 ml of benzene, and 1 ml of pyridine. With stirring and cooling with water, to the reaction mixture was added 1.8 ml of thionyl chloride at such a rate that the temperature of the reaction mixture did not rise above 20°. The precipitate gradually dissolved. The reaction mixture was stirred for 30 min and then carefully heated to boiling on a water bath. The solution then became turbid and a second layer separated. The mixture was boiled for 10-15 min and cooled, warm water added, and the mixture stirred and transferred to a separatory funnel. The benzene layer was separated, washed three times with warm water, and dried over sodium sulfate, and the benzene removed by distillation. The residue was dissolved in hot alcohol and treated with activated charcoal and the filtrate left to crystallize. We obtained 3.45 g of  $\alpha$ -benzenesulfonamido- $\beta$ -chloropropiofenone as square, colorless platelets with m. p. 103-104°. A further 0.55 g of material was isolated from the mother liquor by partial evaporation. The total yield was 4.0 g (61.7%). For analysis, the substance was recrystallized twice from alcohol, when it had m. p. 106-107°. The substance was insoluble in water, but soluble in organic solvents.

Found %: N 4.37; Cl 10.71.  $\text{C}_{15}\text{H}_{14}\text{O}_3\text{NSCl}$ . Calculated %: N 4.35; Cl 10.95.

$\alpha$ -Benzenesulfonamidoacrylophenone (IV). To a solution of 3.2 g of  $\alpha$ -benzenesulfonamido- $\beta$ -chloropropiofenone (III) in 10 ml of benzene was added 1.6 g of pyridine. The solution was boiled on a water bath for 1 hr. A precipitate formed, and this was collected when the reaction mixture had cooled, and washed with water and alcohol. We obtained 2.0 g of  $\alpha$ -benzenesulfonamidoacrylophenone as a yellowish crystalline product



with m. p. 127-129°. A further 0.5 g of the same substance was isolated from the benzene mother liquor. The total yield was 2.5 g (87.1%). After recrystallization from alcohol, the substance melted at 130-131°. It was insoluble in water, but dissolved in dilute aqueous solutions of sodium hydroxide to form the sodium salt. It decolorized solutions of bromine and potassium permanganate.

Found %: C 62.92; H 4.46; N 4.81; S 11.09.  $C_{15}H_{13}O_3NS$ . Calculated %: C 62.70; H 4.56; N 4.87; S 11.16.

1-Benzenesulfonyl-2-benzoylaziridine (V). a) To 200 ml of a 1% aqueous solution of sodium hydroxide was added 10 g of powdered  $\alpha$ -benzenesulfonamido- $\beta$ -chloropropiophenone (III). The reaction mixture was stirred. At first there was appreciable solution of the precipitate, but fine acicular crystals soon separated and the reaction mixture changed to a difficultly stirrable suspension. The mixture was left for 30 min and then the precipitate collected and washed with water and alcohol. We obtained 5.4 g (60.6%) of 1-benzenesulfonyl-2-benzoylaziridine with m. p. 126.5-127°. After recrystallization from alcohol, the needles had m. p. 129-130°.

Found %: C 62.72; H 4.61; N 5.00; S 10.70.  $C_{15}H_{13}O_3NS$ . Calculated %: C 62.70; H 4.56; N 4.87; S 11.16.

Acidification of the aqueous mother solution with hydrochloric acid yielded 3.25 g (36.5%) of  $\alpha$ -benzenesulfonamidoacrylophenone (IV) with m. p. 129-130°. The substance did not depress the melting point of the  $\alpha$ -benzenesulfonamidoacrylophenone obtained in the previous experiment with pyridine.

b) Under the conditions of the previous experiment, from 1 g of  $\alpha$ -chloro- $\beta$ -benzenesulfonamidopropiophenone (VI) we obtained 0.71 g (80%) of 1-benzenesulfonyl-2-benzoylaziridine. No  $\beta$ -benzenesulfonamidoacrylophenone was isolated from the aqueous mother solution.

$\alpha$ -Chloro- $\beta$ -benzenesulfonamidopropiophenone (VI). A 2.0-g sample of 1-benzenesulfonyl-2-benzoylaziridine (V) was added to a solution of 2 ml of concentrated hydrochloric acid in 10 ml of alcohol. The mixture was boiled for 15 min and then left overnight to crystallize. The precipitate was collected, washed with 50% alcohol, and dried. We obtained 1.6 g of  $\alpha$ -chloro- $\beta$ -benzenesulfonamidopropiophenone with m. p. 87-89°. A further 0.46 g of the substance was obtained from the mother solution by dilution with water. The total yield was 2.06 g (90.7%). On recrystallization from alcohol, the substance formed lustrous platelets with m. p. 92-93°. The compound depressed the melting point of  $\alpha$ -benzenesulfonamido- $\beta$ -chloropropiophenone (III).

Found %: C 55.71; H 4.37; N 4.38; Cl 10.94; S 10.04.  $C_{15}H_{14}O_3NSCl$ . Calculated %: C 55.75; H 4.35; N 4.35; Cl 10.95; S 9.90.

$\alpha$ -Benzenesulfonylmethylamidoacrylophenone (VII). Into a flask with a stirrer and thermometer were placed 2.9 g of  $\alpha$ -benzenesulfonamidoacrylophenone (IV) and 30 ml of a 3% solution of sodium hydroxide. The reaction mixture was stirred at 30°; the precipitate dissolved to form a yellow solution, but the  $\alpha$ -benzenesulfonamidoacrylophenone then precipitated partially as the sodium salt. To the mixture was added 1.0 ml of dimethyl sulfate, the mixture stirred at 30-35° for 10 min, and then a further 0.8 ml of dimethyl sulfate added. The reaction mixture was stirred for 1 hr at the same temperature and the precipitate then collected and washed with water. We obtained 2.23 g of a yellowish crystalline substance with m. p. 120-122°, which was recrystallized from alcohol. The yield of  $\alpha$ -benzenesulfonylmethylamidoacrylophenone was 1.5 g (74%) and the m. p. was 126-127°. The substance depressed the melting point of the starting  $\alpha$ -benzenesulfonamidoacrylophenone.

Found %: C 63.97; H 5.01; N 4.73.  $C_{16}H_{15}O_3NS$ . Calculated %: C 63.75; H 5.01; N 4.64.

Benzoylacetyl (VIII). A mixture of 5.74 g of  $\alpha$ -benzenesulfonamidoacrylophenone (IV), 25 ml of alcohol, and 1 ml of 40% sulfuric acid solution was boiled on a water bath for 1 hr. Then 15 ml of alcohol was removed in vacuum at 40-45°. The residue deposited crystals on cooling. They were collected and washed with water. We obtained 2.4 g of benzenesulfonamide with m. p. 152-157°. The substance did not depress the melting point of authentic benzenesulfonamide. The alcohol mother solution was diluted with water and extracted with benzene. The benzene solution was dried over calcium chloride, the benzene removed, and the residue vacuum distilled. We obtained 2.65 g (89.2%) of benzoylacetyl with b. p. 98-99° (11 mm),  $n_D^{22}$  1.5328 (according to literature data [5]; b. p. 101.6-102.6° at 12 mm,  $n_D^{10}$  1.537).

Under the same conditions,  $\alpha$ -benzenesulfonylmethylamidoacrylophenone (VII) decomposed completely to benzoylacetyl and benzenesulfonylmethylamide, while  $\alpha$ -benzenesulfonamido- and  $\alpha$ -benzenesulfonylmethylamido- $\beta$ -hydroxypropylophenones remained unchanged.

## SUMMARY

1. We synthesized and characterized  $\alpha$ -benzenesulfonamido- and  $\alpha$ -benzenesulfonylmethylamidoacrylophenones, which are the most probable intermediates in the conversion of the corresponding  $\alpha$ -benzenesulfonamido- $\beta$ -hydroxypropiofenones into benzoylacetyl.

2. It was shown that the rate of cleavage of  $\alpha$ -benzenesulfonamidoacrylophenones to benzoylacetyl and the corresponding benzenesulfonamide is many times greater than the rate of cleavage of  $\alpha$ -benzenesulfonamido- $\beta$ -hydroxypropiofenones.

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SOME REACTIONS OF BIS( $\beta$ -HYDROXYETHYL)-  
AMINO-*p*-BENZOQUINONE. II\*\*

A. Ya. Berlin and A. N. Makarova

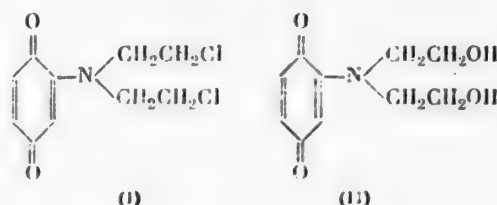
Institute of Experimental and Clinical Oncology, Academy of Medical Sciences, USSR

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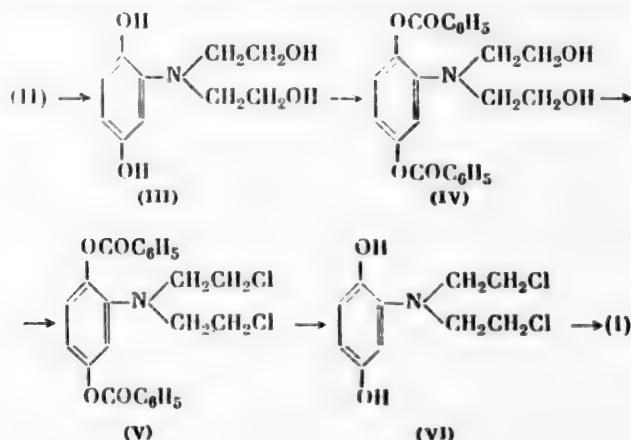
November, 1960

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In searches for new substances with antitumor activity, it seemed interesting to us to synthesize bis( $\beta$ -chloroethyl)-amino-*p*-benzoquinone (I) from bis( $\beta$ -hydroxyethyl)-amino-*p*-benzoquinone (II), which we prepared previously.



All attempts to replace the hydroxyl groups in compound (II) by chlorine atoms by the action of thionyl chloride under various conditions were unsuccessful, as there was always considerable tar formation, and no individual substance could be isolated from the reaction mixture. Assuming that the reason for the failure of these experiments was the presence of the extremely reactive *p*-benzoquinone residue in the molecule, we attempted to effect this synthesis through the corresponding hydroquinone by the following scheme:



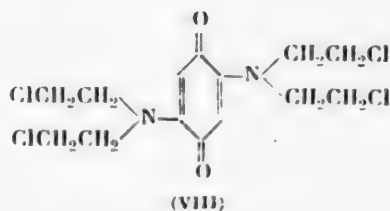
\* For communication I, see [1].

Quinone (II) was converted into hydroquinone (III) by catalytic hydrogenation. When Raney nickel was used in alcohol, it was impossible to isolate pure hydroquinone (III) as the substance was oxidized extremely readily in air to the starting benzoquinone (II), and therefore the hydrogenation was carried out in water in the presence of a platinum catalyst, and the colorless solution of hydroquinone (III) obtained was immediately treated with alkali and benzoyl chloride to form 2,5-dibenzoyloxy-bis( $\beta$ -hydroxyethyl)-aniline (IV). By the action of thionyl chloride, the dibenzoate (IV) was readily converted into 2,5-dibenzoyloxy-bis( $\beta$ -chloroethyl)-aniline (V).

However, it was impossible to isolate the hydroquinone (VI) and the quinone (I). Heating the dibenzoate (V) with alcoholic hydrochloric acid formed an uncrystallizable red-violet mass, and in only one experiment we obtained a very small amount of cherry-red crystals, which were apparently 2-chloro-5-bis( $\beta$ -chloroethyl)-amino-p-benzoquinone (VII), which was formed as a result of successive hydrolysis, oxidation, and addition of hydrogen chloride.

From the amount of benzoic acid formed, it was shown indirectly that the action of 90% sulfuric acid on the dibenzoate (V) at room temperature produced practically complete hydrolysis of the benzoyloxy group, but all attempts to oxidize the hydrolysis product of (V) with p-benzoquinone,  $H_2O_2$ ,  $Ag_2O$ ,  $PbO_2$  [2],  $O_2$ , etc., were unsuccessful.

Bis( $\beta$ -chloroethyl)-amino-p-benzoquinone (I) was recently described as a by-product in the synthesis of compound (VIII) by condensation of p-benzoquinone with bis(1-chloroethyl)-aniline [3].



## EXPERIMENTAL

2,5-Dibenzoyloxybis( $\beta$ -hydroxyethyl)-aniline (IV). A 0.5-g sample of bis( $\beta$ -hydroxyethyl)-amino-p-benzoquinone was dissolved in 50 ml of hot distilled water and the solution cooled to room temperature. Hydrogenation was carried out in the presence of 0.1 g of  $PtO_2 \cdot H_2O$  until a colorless solution was formed, and 85 ml of hydrogen (22°, 730 mm) was thereupon absorbed. At the end of the reaction, the catalyst was allowed to settle, the colorless solution rapidly decanted from it, an aqueous solution of 0.228 g of NaOH and 0.6 ml of distilled benzoyl chloride were added, and the mixture was shaken with cooling in a stream of water. The gray precipitate was collected and dried. The weight was 0.7 g. Recrystallization from benzene yielded colorless crystals with m. p. 151-152°.

Found %: C 68.46, 68.76; H 5.42, 5.63; N 3.43;  $H_{act}$  0.58, 0.55.  $C_{24}H_{23}O_6N$ . Calculated %: C 68.41; H 5.51; N 3.33;  $H_{act}$  0.48.

The quinone (II) could also be hydrogenated as a suspension in water.

2,5-Dibenzoyloxy-bis( $\beta$ -chloroethyl)-aniline (V). To 0.4 g of the dibenzoate (IV) was added 4 ml of thionyl chloride and the greenish yellow solution formed left overnight at room temperature. The excess thionyl chloride was removed in vacuum in the cold with the addition and vacuum distillation of two 5 ml portions of absolute ether. The residue was a yellowish crystalline mass (0.4 g, 93%) with m. p. 105-107°. Two recrystallizations from alcohol yielded colorless crystals with m. p. 110-110.5°. The substance was readily soluble in the normal organic solvents, but sparingly soluble in hexane.

Found %: C 62.38; H 4.68; Cl 15.22.  $C_{24}H_{21}O_4NCl_2$ . Calculated %: C 62.80; H 4.62; Cl 15.50.

Hydrolysis and oxidation of the dichloride (V). a) Action of alcoholic hydrochloric acid. A mixture of 0.1 g of the dichloride (V), 3 ml of concentrated hydrochloric acid, and 5 ml of alcohol was heated in a sealed tube at 125-130° for 6.5 hr. The dark violet solution formed did not deposit a precipitate either on cooling or on gradual evaporation and cooling. The residue after complete removal of the solvent was a dark cherry red, thick, tarry mass, which was readily soluble in alcohols, but insoluble in ether, benzene, and hexane. The

substance was dissolved in a small amount of alcohol and precipitated with ether. The turbid pink solution formed was decanted from the tar deposited on the walls and left in a refrigerator. By next day the solution had deposited a small amount of dark cherry red, well formed, dense crystals of 2-chloro-5-bis( $\beta$ -chloroethyl)-amino-p-benzoquinone (VII) with m. p. 175-177°.

Found %: C 41.98; H 5.03; Cl 34.5.  $C_{16}H_{10}O_2NCl_2$ . Calculated %: C 42.48; H 3.58; Cl 37.7.

It was not possible to purify the substance further because of the small amount of it.

b) Action of 90% sulfuric acid. A 0.1-g sample of the dichloride (V) was dissolved in 5 ml of 90% sulfuric acid without heating. The next day the brown liquid was poured into 50 ml of ice water and the aqueous solution extracted with three 20-ml-portions of ether. The combined ether extracts were washed with three 5-ml portions of water (until the acid reaction to Congo disappeared), the ether evaporated, and the benzoic acid in the residue determined potentiometrically (2.03 equiv. were found). In a control experiment under the same conditions, but with a sample of pure benzoic acid, 98% of the acid taken was found.

None of the numerous attempts to oxidize the hydrolysis product, both as a mixture with benzoic acid and with preliminary removal of the latter by the action of various oxidants such as p-benzoquinone,  $H_2O_2$ ,  $Ag_2O$ , activated  $PbO_2$ , atmospheric oxygen, etc., led to the quinone (I). Interesting us, though in most cases the ether or ethyl acetate solution, which was originally colorless, acquired an orange color on oxidation.

All the analyses were carried out in the analytical chemistry laboratory of the Institute under the direction of A. D. Chirnaeva.

#### SUMMARY

1. 2,5-Dibenzoyloxy-bis( $\beta$ -hydroxyethyl)-aniline and 2,5-dibenzoyloxy-bis( $\beta$ -chloroethyl)-aniline were obtained from bis( $\beta$ -hydroxyethyl)-amino-p-benzoquinone.

2. Attempts at the hydrolysis of 2,5-dibenzoyloxy-bis( $\beta$ -chloroethyl)-aniline with subsequent oxidation were unsuccessful.

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## AMINOCOLCHICIDE AND ITS DERIVATIVES

### II. AMINODESACETYL-N-METHYLCOLCHICIDE

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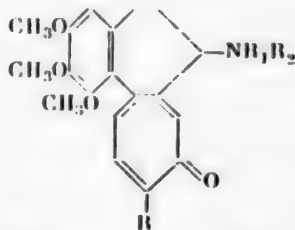
Original article submitted January 1, 1960

The preparation of aminodesacetylcolchiclide (I) from aminocolchiclide (II) was described in a previous communication [1]. The next step in the investigation was the preparation of two N-methyl derivatives of aminodesacetylcolchiclide.

Aminodesacetyl-N-methylcolchiclide (III), which could be called the amide of colchameine, was prepared by the action of aqueous ammonia on colchamine (IV) in methanol [2], by heating colchamine or colchameine (V) with ammonia under pressure [3], and by the action of strong ammonia on colchameine at room temperature [4]. It is noteworthy that there is a substantial difference in literature data on the constants of aminodesacetyl-N-methylcolchiclide (see table).

In the case of the melting point, these discrepancies are partly explained by the effect of the solvents used for recrystallization [4].

The product (II) was obtained by the action of strong aqueous ammonia on colchamine at room temperature. Products which differed strongly in melting point were isolated in different experiments. It was found that too short a treatment with ammonia yielded an intermediate product, which was probably a molecular compound of colchamine (IV) and aminodesacetyl-N-methylcolchiclide (III).



- |   |   |
|---|---|
| (I) $R = \text{NH}_2$ , $R_1 = R_2 = \text{H}$ ;                    | (VI) $R = \text{OCH}_3$ , $R_1 = R_2 = \text{CH}_3$ ; |
| (II) $R = \text{NH}_2$ , $R_1 = \text{H}$ , $R_2 = \text{COCH}_3$ ; | (VII) $R = \text{OCH}_3$ , $R_1 = R_2 = \text{H}$ ;   |
| (III) $R = \text{NH}_2$ , $R_1 = \text{H}$ , $R_2 = \text{CH}_3$ ;  | (VIII) $R = \text{OH}$ , $R_1 = R_2 = \text{CH}_3$ ;  |
| (IV) $R = \text{OCH}_3$ , $R_1 = \text{H}$ , $R_2 = \text{CH}_3$ ;  | (IX) $R = \text{NH}_2$ , $R_1 = R_2 = \text{CH}_3$ ;  |
| (V) $R = \text{OH}$ , $R_1 = \text{H}$ , $R_2 = \text{CH}_3$ ;      |   |

Both substances were detected in this product by paper chromatography, and its analysis corresponded to the formula  $\text{C}_{41}\text{H}_{49}\text{O}_9\text{N}_3$ , which is the sum of  $\text{C}_{21}\text{H}_{25}\text{O}_5\text{N}$  (IV) and  $\text{C}_{20}\text{H}_{24}\text{O}_4\text{N}_2$  (III).

In the colchicine series there is a case of the formation of a similar molecular compound: The reaction of colchicine and colchamine forms colchicerine, which is a molecular compound of the two alkaloids named [6, 7]. Colchicerine is obtained readily the reaction of colchamine and colchicine, and its melting point is



Recrystallization solvent	Melting point	Specific rotation			Literature reference
		$[\alpha]_D^{25}$	concentration	solvent	
Methanol	120-122°	-126 <sup>25</sup>	1.072	Chloroform	[5]
	128-131 (decomp.)	-131 <sup>22</sup>			[2]
Ethyl acetate	198-200	-17±3		Chloroform	[3]
Ethyl acetate	198-200	-17±3		Chloroform	[4]
Water	120-125				[4]

higher than that of either of the substances forming it. The molecular weight of colchicine found cryoscopically corresponds to the calculated value for the molecular compound.

In our case, determination of the molecular weight cryoscopically showed that the molecular compound (III)-(IV) hardly exists in benzene solution. The molecular weight found corresponded to only a relatively insignificant number of large molecules with the calculated molecular weight of 727. The preparation of the intermediate product by mixing the substances forming it was found to be difficult, and it melted below the components. It is possible that the product examined was not a molecular compound, but mixed crystals.

The intermediate product could not be isolated in any experiment where the treatment time was longer than 2 days. In all these cases we obtained aminodesacetyl-N-methylcolchicine (III), which gave different crystal forms on recrystallization. One form, which consisted of fine needles, was obtained from relatively dilute solutions, while the other, which consisted of refracting platelets, was isolated by slow concentration of solutions.

The contradictory data on the melting point of aminodesacetyl-N-methylcolchicine (III) evidently may be explained in various ways.

It is a different case with the difference in the data on the specific rotation. This problem has been studied for colchicine [8]. In chloroform, the absolute value of the specific rotation falls with an increase in the colchicine concentration. The absolute value of the specific rotation of colchicine in alcohol is higher than in chloroform and is independent of concentration. The absolute value of the specific rotation increases with the addition of alcohol to chloroform.

We observed analogous phenomena for aminocolchicine (II). Over a narrow range of concentrations there was a linear relation between the specific rotation of aminocolchicine and the concentration at 18-20°, which could be expressed by the formula

$$[\alpha]_D = -[71(1.071 - c) + 100]^\circ,$$

where  $c$  is the concentration in the range 0.300-0.700 g of substance/100 ml of solution.

The specific rotation of aminocolchicine in alcohol was considerably higher and independent of concentration.

In the case of aminodesacetyl-N-methylcolchicine (III), no substantial changes in specific rotation with concentration were observed. There was no appreciable difference in the specific rotations of alcohol and chloroform solutions. Therefore, it is not yet possible to draw any conclusions on the reasons for the difference in literature data. The specific rotation presented in the first line of the table agrees with our data.

It was shown previous that methylation by the Leuckart-Wallach method is applicable in the colchicine series [2, 29, 10]. In the methylation of colchamine (IV), the yield of N-methylcolchamine (VI) was ~80%, while N-methylcolchamine was obtained in about 50% yield from desacetylcolchicine (VII); approximately 40% of N-methylcolchamine (VIII) was formed from colchamine (V). We methylated aminodesacetylcolchicine with formalin and formic acid and obtained aminodesacetyl-N-dimethylcolchicine (IX) in 37% yield. For identification, the same product was prepared by the reaction of N-methylcolchamine with ammonia.

Aminodesacetyl-N-dimethylcolchiclide (IX) has a strange property: The melting point of crystals of it obtained from ethyl acetate increased after careful grinding.

We are very grateful to L. M. Utkin for continuous interest in the work and G. G. Dvoryantseva for determining the molecular weight.

#### EXPERIMENTAL

Reaction of colchamine (IV) with ammonia. A solution of 1 g of colchamine in 7.5 ml of alcohol was mixed with 42.5 ml of an aqueous solution of ammonia (d 0.904); after 16.5 hr, the solution was extracted with chloroform. The residue from the extract was dissolved in 2 ml of ethyl acetate. On standing, the solution deposited 0.73 g of refracting, laminar crystals with m. p. 155-157°. The melting point was unchanged after the material had been recrystallized from ethyl acetate. For analysis, the substance was dried for 8 hr at 3 mm and 100°.  $[\alpha]^{19}_D -121.9^\circ$  (c 0.998, chloroform);  $-128.4^\circ$  (c 0.853, alcohol).

Found %: N 5.54; OCH<sub>3</sub> 30.09, 29.58. C<sub>44</sub>H<sub>49</sub>O<sub>3</sub>N<sub>3</sub>. Calculated %: N 5.78; OCH<sub>3</sub> 29.85.

In other experiments, the product obtained melted at 142-144°. The molecular weight of this substance, found cryoscopically in benzene, was 414.

Aminodesacetyl-N-methylcolchiclide (III). A solution of 1.12 g of colchamine in 10 ml of alcohol was mixed with 47.5 ml of an aqueous solution of ammonia (d 0.904). After 3 days, the mixture was extracted with chloroform. The residue from the extract was dissolved in 1.5 ml of ethyl acetate. We obtained 0.88 g of crystals in the form of needles grouped in rosettes with m. p. 122-125°. After recrystallization from ethyl acetate, the substance softened at 143-144°, then solidified and melted at 198-200°. When the solvent was evaporated from the mother solution slowly, platelets with m. p. 127-130° appeared on the bottom and walls of the flask. On recrystallization, this substance gave needles with m. p. 198-200°. Recrystallization of the latter gave platelets from the mother solution in addition to the substance with the same melting point.

Aminodesacetyl-N-methylcolchiclide with m. p. 198-200° was also obtained by the action of ammonia on the intermediate product described above.

In chloroform  $[\alpha]^{20}_D -126.9^\circ$  (c 0.420);  $[\alpha]^{19}_D -128.2^\circ$  (c 0.721) and  $-125.6^\circ$  (c 1.144). In alcohol  $[\alpha]^{19}_D -123.4^\circ$  (c 0.285);  $-1123.6^{**}$  (c 1.065).

The hydrochloride had m. p. 271° (decomp., from alcohol). It was readily soluble in water.

In water  $[\alpha]^{17}_D -242.1^\circ$  (c 0.740);  $[\alpha]^{18}_D -257.8^\circ$  (c 0.741);  $[\alpha]^{19}_D -269.0^\circ$  (c 0.751);  $[\alpha]^{21}_D -277.8^\circ$  (c 0.770). These solutions had pH ~5.5.

Found %: C 61.37, 60.51; H 6.26, 6.60; N 7.25; Cl 8.91. C<sub>20</sub>H<sub>24</sub>O<sub>4</sub>N<sub>2</sub>·HCl. Calculated %: C 61.10; H 6.42; N 7.13; Cl 9.03.

Liberation of the free base from the hydrochloride yielded both crystal forms of aminodesacetyl-N-methylcolchiclide.

Aminodesacetyl-N-dimethylcolchiclide (IX). a) A mixture of 7.73 g of aminodesacetylcolchiclide (I), 20 ml of 31.5% formalin, and 10 ml of 85% formic acid was heated on a boiling water bath for 30 min. The cooled mixture was diluted with 50 ml of water, made alkaline with 90 ml of 12% NaOH, and extracted with chloroform. The residue from the extracts was recrystallized from ethyl acetate. We obtained 3.10 g of compound (IX), and recrystallization of this from the same solvent with charcoal gave 2.44 g of product; the substance consisted of fine yellow needles with m. p. 201-203°; if the crystals were ground carefully, the m. p. was 222-224°. This phenomenon could be observed with carefully purified material, preferably after purification through the hydrochloride. In one experiment, N-methylcolchamine (VIII) was isolated from the mother solution after separation of compound (IX).

For chloroform solutions of compound (IX):  $[\alpha]^{17}_D -67.6^\circ$  (c 0.324);  $[\alpha]^{20}_D -70.7^\circ$  (c 0.760).

Found %: N 7.32, 7.37; OCH<sub>3</sub> 24.28, 23.67; NCH<sub>3</sub> 8.07. C<sub>21</sub>H<sub>26</sub>O<sub>4</sub>N<sub>2</sub>. Calculated %: N 7.52; OCH<sub>3</sub> 24.01; NCH<sub>3</sub> 7.84.

\* As in original - Publisher.

The hydrochloride had m. p. 274-275° (decomp., from alcohol). It was readily soluble in water.

In water  $[\alpha]^{18}_D -134.1^\circ$  (c 0.334);  $-196.2^\circ$  (c 0.558);  $-272.4^\circ$  (c 1.156).

Found %: C 61.65, 61.85; H 6.62, 6.52; N 6.66, 6.67; Cl 8.74, 8.72.  $C_{21}H_{28}O_4N_2 \cdot HCl$ . Calculated %: C 61.95; H 6.69; N 6.89; Cl 8.72.

b) A solution of 2.5 g of N-methylcolchamine (VI) in 25 ml of alcohol was mixed with 120 ml of an aqueous ammonia solution (d 0.909). A crystalline precipitate appeared after 1 hr. After 3 days, the precipitate was collected and washed with water (yield 1.70 g). Recrystallization from ethyl acetate yielded 1.24 g of compound (IX) as fine yellow needles with m. p. 199-204°. A further 0.48 g of compound (IX) was obtained from the mother solution.

In chloroform  $[\alpha]^{21}_D -70.5^\circ$  (c 0.353);  $[\alpha]^{19}_D -78.7^\circ$  (c 0.696).

Found %: N 7.42.  $C_{21}H_{26}O_4N_2$ . Calculated %: N 7.52.

The identity of the substances obtained by the two methods was evident from the properties, the fact that a mixed melting point was not depressed, and the correspondence of the ultraviolet and infrared absorption spectra. The hydrochlorides of the bases obtained by methods a) and b) were found to be identical.

Specific rotation of aminocolchicid (II). For dehydration of the crystal hydrate of (II), the substance was dried over  $P_2O_5$  for 9 hr at 3 mm and 100°; the weight loss was 9.69%. The substance was then dried for 7 hr at 3 mm and 135°.

Found %:  $H_2O$  11.58.  $C_{21}H_{24}O_5N_2 \cdot 3H_2O$ . Calculated %:  $H_2O$  12.33.

The crystal hydrate of (II) was recrystallized from chloroform. We obtained a product with m. p. 259-260°. The substance was dried for 30 hr at 3 mm and 135°.

Found %:  $CHCl_3$  13.01, 13.10.  $C_{21}H_{24}O_5N_2 \cdot \frac{1}{2}CHCl_3$ . Calculated %:  $CHCl_3$  13.46.

The specific rotations of chloroform solutions of compound (II) containing chloroform of crystallization were as follows:  $[\alpha]^{19}_D -148.6^\circ$  (c 0.362);  $[\alpha]^{20}_D -137.2^\circ$  (c 0.542);  $[\alpha]_D -130.5^\circ$  (c 0.677). The values calculated from the formula (p. 3687) were  $[\alpha]_D -150.2^\circ$ ,  $-137.6^\circ$ ,  $-127.9^\circ$ , respectively, for the three concentrations.

In alcohol  $[\alpha]^{18}_D -250.0^\circ$  (c 0.236),  $[\alpha]^{20}_D -256.3^\circ$  (c 0.244),  $-256.4^\circ$  (c 0.480),  $-252.3^\circ$  (c 0.741),  $-252.8^\circ$  (c 0.793).

## SUMMARY

1. Aminodesacetyl-N-methylcolchicid (amide of colchameine) forms a compound with colchamine, which is apparently a molecular compound.
2. Aminodesacetyl-N-dimethylcolchicid was prepared.
3. The specific rotation of aminocolchicid in chloroform and alcohol was studied over a narrow range of concentrations.

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# MECHANISM OF THE OXIDATION OF AROMATIC AMINES AND NITROSO COMPOUNDS BY CARO'S ACID

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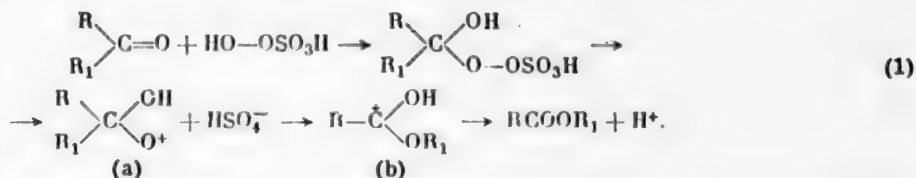
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November, 1960

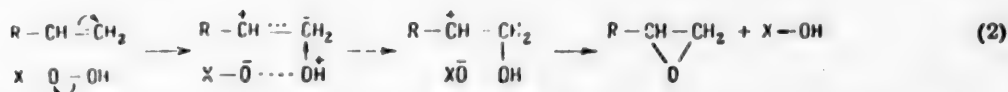
Original article submitted January 4, 1960

Caro's acid is often used in organic synthesis as an oxidant for converting cyclic ketones into lactones and ketones with an open chain into esters (Baeyer-Villiger reaction [1]), for the oxidation of amines to nitroso compounds [2-4], for the preparation of amine oxides, iodo compounds, etc. [5]. The mechanism of oxidation by Caro's acid has been studied in detail only for the Baeyer-Villiger reaction [6-8] and scheme (1) was substantiated quite well.



According to this scheme, the unstable ion (a) is formed with rupture of the peroxide bond and rearranges very rapidly to the ion (b) with the transfer to oxygen of the radical R or R<sub>1</sub> which can most readily acquire a negative charge. This explains the observed direction of the bond rearrangement.

Among the reactions of other peracids, a detailed investigation has been made of the conversion of olefins and their derivatives into oxides (Prilezhaev reaction) for which mechanism (2) was proposed [5, 9, 10].



This explains the activating effect of electron-donor substituents in the olefin molecule and the passivating effect of electron-acceptor substituents.

Both mechanisms presented assume polarization of the peroxide bond -O-O and its heterolytic rupture.

However, there is another possibility for explaining the mechanism of oxidation by Caro's acid and other peracids, namely, decomposition to the free radicals HO<sup>•</sup> and HSO<sub>4</sub><sup>•</sup>, which act as oxidants. The possibility of this course for the reactions examined agrees with the fact that many reactions of hydrogen peroxide [5] and other peroxide compounds proceed by a radical mechanism. For example, it was shown with the aid of the heavy oxygen isotope O<sup>18</sup> that potassium persulfate in aqueous solution oxidizes by the transfer of electrons, evidently with the intermediate formation of the radical-ion SO<sub>4</sub><sup>•-</sup>, which also acts as an oxidant [11-13]. The participation of free radicals is also assumed in some stages of the oxidation of amines by peracids [14].

In the present work we used isotopes to distinguish between the heterolytic schemes for oxidation by Caro's acid of type (1) or (2) and the radical mechanism. We studied the oxidation of aromatic amines to nitroso compounds and the latter to nitro compounds by the potassium salt of normal Caro's acid in water labeled with heavy oxygen  $\text{H}_2\text{O}^{18}$ .

With radical decomposition of Caro's acid, the radicals  $\text{HO}^\bullet$  and  $\text{SO}_4^{\bullet-}$  formed should undergo fast reactions [11-13, 15]:



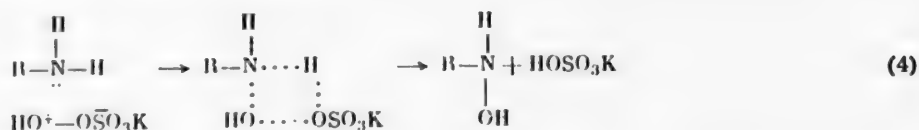
which lead to replacement of radicals from the oxidant  $\text{HO}^{18}$  radicals from water. The latter act as the main source of oxygen in the oxidation products. Thus, these products should contain excess  $\text{O}^{18}$  if the oxidation proceeds by a radical mechanism.

With the heterolytic mechanisms, the reaction products should not contain excess  $\text{O}^{18}$ , as peroxide compounds do not exchange their oxygen with water, and exchange should not occur for the  $\text{OH}^+$  group, even if it is formed as a kinetically free ion (which is extremely improbable).

We found that nitrosobenzene, o-nitrosoanisole, p-nitrosobenzene, and p,p'-dinitroazobenzene obtained by oxidation of aniline, o-anisidine, and p-nitroaniline did not contain excess  $\text{O}^{18}$ . It was also absent from nitrobenzene and o-nitroanisole obtained by oxidation of nitrosobenzene and o-nitrosoanisole.

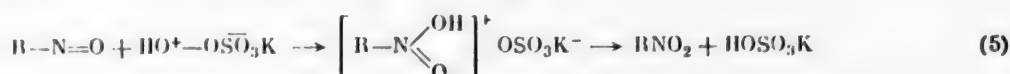
These data are incompatible with the radical mechanism, but correspond to a heterolytic mechanism, which may be represented by schemes (4) and (5) in the cases examined.

For the oxidation of amines to nitroso compounds:



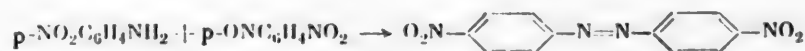
(with subsequent oxidation of the arylhydroxylamine and elimination of water from the nitroso compound hydrate formed).

For the oxidation of nitroso compounds to nitro compounds:



In accordance with the latter scheme, we found that in contrast to nitrosobenzene and nitrosoanisole, p-nitrosobenzene is not oxidized by Caro's acid at room temperature. This retardation of the reaction was to be expected, due to the reduction in the nucleophilicity of the nitroso group nitrogen under the action of the nitro group in the para position.

p,p'-Dinitroazobenzene, which was formed together with p-nitrosobenzene in the oxidation of p-nitroaniline, was probably obtained by the following reaction:



with subsequent oxidation of p,p'-dinitroazobenzene by a mechanism analogous to (5) or (2) with rearrangement of the epoxide formed.

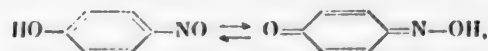
As is clear from the argument presented, the conclusion that the oxidations studied are heterolytic is based on literature data on the rapidity of reaction (3).

In addition to the oxidation mechanism, in the present work we studied the isotopic exchange of nitrobenzene, nitromethane, and a series of nitroso compounds with  $\text{H}_2\text{O}^{18}$ . There are no data on this exchange. We needed them for investigating the oxidation, but they were also of interest in themselves.



It was found that the nitro compounds mentioned do not exchange oxygen with water, even under drastic conditions in the presence of alkali or acid. Among the nitroso compounds, nitrosobenzene, p-nitrosodimethylaniline, o-nitrosoanisole, and p-nitrosanitrobenzene did not exchange in neutral, acid, or alkaline media at temperatures up to 100°, while p-nitrosophenol and  $\alpha$ -nitroso- $\beta$ -naphthol exchanged rapidly even at 50° in the presence of acid ( $\alpha$ -nitroso- $\beta$ -naphthol also in the presence of alkali). Only one of the two oxygen atoms participated in the exchange of the last two compounds.

These data show that even under drastic conditions the nitroso group does not exchange with water and that the exchange in the last two substances occurs only in the hydroxyl group. It occurs in the quinone oxime tautomer



for which, in analogy with carbonyl compounds, one might expect rapid exchange of oxygen in the grouping  $> \text{C} = \text{O}$ .

It is interesting to compare the lack of exchange in the nitroso group with the rapid exchange in the carbonyl group [16], which shows a certain similarity in chemical behavior. This sharp difference in exchange capacity must be explained by the considerably lower polarity of the  $-\text{N}=\text{O}$  group in comparison with the  $> \text{C}=\text{O}$  group, which prevents reversible hydration that leads to isotopic exchange in the case of the carbonyl group.

#### EXPERIMENTAL

Caro's acid [17]. A mixture of 20 g of finely powdered potassium persulfate and 13 ml of concentrated sulfuric acid was ground in a mortar cooled with ice and salt. After 1 hr, the mixture was added to 50 ml of water containing 2.1% excess  $\text{O}^{18}$ , which was partly frozen and cooled with ice and salt. The Caro's acid was then neutralized slowly with a solution of 36 g of freshly baked potassium carbonate in 34 ml of  $\text{H}_2\text{O}^{18}$ , filtered, the precipitate washed with 5 ml of  $\text{H}_2\text{O}^{18}$  and the filtrate diluted to 100 ml with  $\text{H}_2\text{O}^{18}$ . The active oxygen content of the solution obtained was determined by the procedure in [18].

Oxidation of aniline to nitrosobenzene [19]. To 11.4 ml of the solution of Caro's acid, containing 0.103 g of active oxygen, at room temperature was gradually added a solution of an equivalent amount of aniline (0.3 g) in 15 ml of  $\text{H}_2\text{O}^{18}$ . After 10 min, the nitrosobenzene formed was collected, pressed out on filter paper, and purified by vacuum sublimation. Its m. p. was 63.5–64.5°, which corresponds to literature data. The yield was ~0.3 g. Isotopic analysis showed that this substance did not contain excess  $\text{O}^{18}$ .

Oxidation of o-anisidine to o-nitrosoanisole [3]. To 39 ml of the solution of Caro's acid, containing 0.352 g of active oxygen, was added a solution of 1.2 ml of glacial acetic acid in 4 ml of  $\text{H}_2\text{O}^{18}$ . The mixture obtained had pH ~2. An ice-cooled emulsion of 1.35 g of o-anisidine in 10 ml of  $\text{H}_2\text{O}^{18}$  was added with cooling in ice and stirring to the mixture over a period of 0.5 min. After 6 min, the o-nitrosoanisole was collected, pressed out on filter paper, and sublimed in vacuum. The yield of the substance that had been sublimed twice was 0.27 g, and the m. p. was 101–102.5° (according to literature data, m. p. 103°). The substance did not contain excess  $\text{O}^{18}$ .

Oxidation of p-nitroaniline to p-nitrosanitrobenzene and p,p'-dinitroazoxybenzene [2]. To 26 ml of the solution of Caro's acid, containing 0.231 g of active oxygen, were added 75 ml of  $\text{H}_2\text{O}^{18}$  and 1 g of finely ground p-nitroaniline, the mixture shaken for 4 hr and then left for a further 40 hr at room temperature, and the precipitate collected, washed twice with  $\text{H}_2\text{O}^{18}$ , and sublimed in vacuum at up to 160° until sublimation ceased. We obtained 0.43 g of sublimate and 0.45 g of residue. The residue was extracted with 20 ml of boiling chloroform. Evaporation of the extract obtained gave 0.31 g of substance, which, after recrystallization from 3.5 ml of anhydrous dioxane, had m. p. 187.5–188.5° and after a second recrystallization, m. p. 189–190°, which corresponds to literature data for p,p'-dinitroazoxybenzene (m. p. 191.5° [2]). The sublimate was resublimed at up to 90° to give a substance with m. p. 110–113°, which, after recrystallization from anhydrous alcohol, had m. p. 117–118° and was pure p-nitrosanitrobenzene (according to literature data, m. p. 118.5–119° [2]). Isotopic analysis showed that neither of the products isolated contained excess  $\text{O}^{18}$ .



# Summary of Experiments on Exchange of Nitroso Compounds and Nitro Compounds with $H_2O^{18}$

Substance	Sample (g)			Catalyst*	Exchange time (min)	Temperature	Characteristics of exchange
	substance	$H_2O^{18}$	alcohol				
$C_6H_5NO$	0.2	2	2	—	3	70°	None
	0.2	2	2	Ac*	5	85	.
	0.2	2	2	Al*	3	85	.
$p-(CH_3)_2NC_6H_4NO$	0.15	2	2	—	60	100	.
	0.15	2	2	Ac*	25	100	.
	0.15	2	2	Al	5	100	.
$p-O_2NC_6H_4NO$	0.07	0.5	1	—	30	100	.
	0.07	0.5	1	Ac	5	100	.
	0.07	0.5	1	Al	5	100	Decomposition
$o-CH_3OC_6H_4NO$	0.07	0.5	1	—	60	100	None
	0.07	0.5	1	Ac	5	100	Decomposition
	0.07	0.5	1	Al	5	100	The same
$p-HOC_6H_4NO$	0.12	2	2	—	60	100	None
	0.06	0.5	1	Ac	5	100	41%
	0.06	0.5	1	Ac	5	50	10%
	0.06	0.5	1	Al	5	100	None
$\beta, \gamma-HOC_{10}H_8NO$	0.2	2	2	—	60	100	The same
	0.2	2	2	Ac*	12	100	43%
	0.18	1	2	Ac	5	80	42%
	0.09	1	2	Ac	5	50	16%
	0.09	0.5	1	Al	5	100	41%
	0.09	1	2	Al	5	50	6%
$C_6H_5NO_2$	6	2	—	Ac*	16 hr	150	None
	6	2	—	Al*	The same	150	.
$CH_3NO_2$	5	2	—	Ac*	29 hr	150	.
	5	2	—	Al*	25 hr	120	.

\* Ac — 0.2 N HCl; Al — 0.2 N NaOH. The symbols Ac\* and Al\* are used for experiments where the concentrations were 0.5 N.

Oxidation of nitrosobenzene to nitrobenzene. A mixture of 1.65 g of finely ground nitrosobenzene and 30 ml of the solution of Caro's acid, containing 0.272 g of active oxygen, was shaken for 2.5 hr, left for 35 hr, and again shaken for 5 hr. The reaction mixture was then extracted with absolute ether, the extract dried with  $CaCl_2$ , the solvent removed, and the nitrobenzene vacuum distilled. Of the two fractions of nitrobenzene with b. p. 115–117° (40 mm) obtained, the first (0.4 g) had a pale green color from traces of nitrosobenzene and  $n_D^{20}$  1.5507. The second (0.4 g) had the normal color of nitrobenzene and  $n_D^{20}$  1.5513 (for pure nitrobenzene,  $n_D^{20}$  1.5524). Isotopic analysis of the second fraction showed that it contained no excess  $O^{18}$ .

Oxidation of o-nitrosoanisole to o-nitroanisole. A mixture of 0.215 g of finely ground o-nitrosoanisole and 7 ml of the solution of Caro's acid, containing 0.030 g of active oxygen, was shaken for 3 hr, left for 35 hr, and again shaken for 5 hr. The o-nitroanisole was isolated analogously to the nitrobenzene and had b. p. 130–135° (10 mm) and  $n_D^{20}$  1.5628. The yield was ~0.1 g (literature data for o-nitroanisole: b. p. 132–133° at 11 mm and  $n_D^{20}$  1.56204, 1.5619 [20]). The substance did not contain excess  $O^{18}$ . The water used to prepare the Caro's acid for this experiment contained 1.1% of excess  $O^{18}$ .

Attempted oxidation of p-nitrosobenzene to p-dinitrobenzene. A mixture of 0.235 g of p-nitrosobenzene and 7 ml of the solution of Caro's acid, containing 0.030 g of active oxygen, was shaken for 3 hr, left for 35 hr, and again shaken for 6 hr. The precipitate was collected, washed twice with  $H_2O^{18}$  and dried, when it had m. p. 109–111°. Sublimation in vacuum at 90° gave a substance with the same melting point as the starting p-nitrosobenzene. There was no involatile residue. These data show that no oxidation occurred.

Investigation of isotopic exchange. The exchange of nitroso compounds was studied in homogeneous aqueous alcohol solution under neutral conditions and in the presence of 0.2–0.5 N HCl or NaOH. The mixture

of the substance, water (containing 1,2 at. % of excess  $O^{18}$ ), and alcohol was heated in a sealed glass ampoule and then the solvent removed and the substance purified by vacuum sublimation. The purity of the starting preparations and the substances isolated after exchange was checked by the melting points, which corresponded to literature data in all cases. The nitrobenzene and nitromethane exchanged with water under heterogeneous conditions. They were separated from the water, dried, and vacuum distilled, and their purity was checked by the boiling points and refractive indices. A summary of the conditions and results of typical experiments is given in the table.

Isotopic analysis was carried out by the method of Rittenberg and Ponticorvo [21], which consists in heating a sample of the substance and mercuric chloride in an evacuated ampoule and analyzing the  $CO_2$  formed mass spectrometrically. In some of the experiments we also used the method in [22] with the use of platinum ampoules.

We would like to thank A. I. Brodskii for help in discussing the results of this work and I. M. Protas for making the mass spectrometric measurements.

### SUMMARY

1. It was shown that nitrosobenzene, o-nitrosoanisole, p-nitrosobenzene, and p,p'-dinitroazobenzene obtained by the action of the potassium salt of Caro's acid in  $H_2O^{18}$  on aniline, o-anisidine, and p-nitroaniline do not contain excess  $O^{18}$ . There was also no excess  $O^{18}$  in nitrobenzene and o-nitroanisole obtained under the same conditions from nitrosobenzene and o-nitrosoanisole, respectively.

2. These data are incompatible with the radical mechanism for the oxidation, but correspond to a heterolytic mechanism, for which possible schemes are proposed.

3. It was found that nitrobenzene and nitromethane do not exchange their oxygen with  $H_2O^{18}$  under drastic conditions in the presence of acid or alkali. Among the series of nitroso compounds studied, only p-nitrosophenol and  $\alpha$ -nitroso- $\beta$ -naphthol exchanged the one oxygen atom of the OH group. The nitroso group did not undergo exchange.

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# SYNTHESIS AND INVESTIGATION OF CYCLOALIPHATIC POLYENE COMPOUNDS

## I. SYNTHESIS OF POLYENE ALDEHYDES OF THE $\Delta^3$ -CYCLOHEXENE SERIES

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Despite the large number of papers on the synthesis and the study of the chemical properties of polyene compounds, interest in them is continually increasing. This is explained not only by the fact that substances with a polyene structure occur widely in nature and consequently their synthesis is of interest in itself, but also by the fact that aliphatic polyene systems with functional groups may be used as intermediates for the synthesis of a large number of natural substances and their analogs containing various carbocyclic systems.

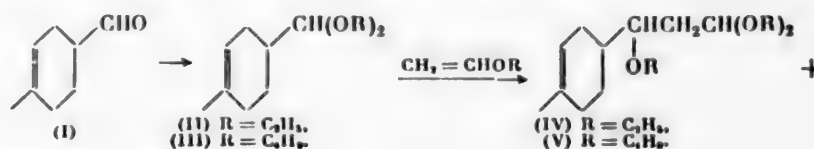
There have now been quite extensive descriptions of the preparation and properties of aliphatic [1-4] and aromatic [5-8] compounds with polyene chains and also cycloaliphatic compounds with the double bond in the cyclohexene ring in position 1. These include aromatic principles [4], vitamin A [1], carotenoids [1], and also some of their analogs. In most cases, natural products are used to prepare these substances.

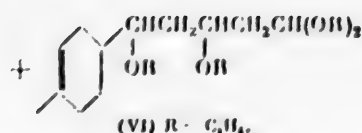
It seemed interesting to investigate cycloaliphatic polyene compounds of the  $\Delta^3$ -cyclohexene series, which have not been studied up to now and may be synthesized from readily accessible products of diene synthesis.

In the present work we started from 4-methyl- $\Delta^3$ -tetrahydrobenzaldehyde (I), which was obtained by diene condensation of isoprene and acrolein.

For the construction of a polyene side chain we chose the condensation of acetals with vinyl ethers, which has previously been used successfully for this purpose by many authors [3, 7, 8, 9, 10]. The best catalyst for the reaction was found to be zinc chloride in ethyl acetate or butyl acetate, but it was necessary to select the reaction conditions in each actual case to obtain a satisfactory yield of primary condensation product.

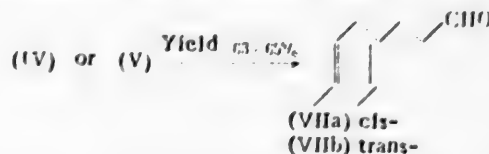
To study the lability of the alkoxy groups in the acetals and to compare the hydrolysis products of ether acetals obtained by this condensation, we used for the first stage of the synthesis the ethyl (II) and butyl (III) acetals of 4-methyl- $\Delta^3$ -tetrahydrobenzaldehyde and the two corresponding vinyl ethers. It was found that with an equimolecular ratio of the starting reagents, the diethyl acetal (II) reacted with vinyl ethyl ether at 70-75° to form about 13% of the primary condensation product (IV), while the dibutyl acetal (III) of the same aldehyde reacted with vinyl butyl ether even at 20-22°, and the yield of the primary condensation product (V) reached 19%. Thus, the acetal with the heavier radical was found to be more reactive.



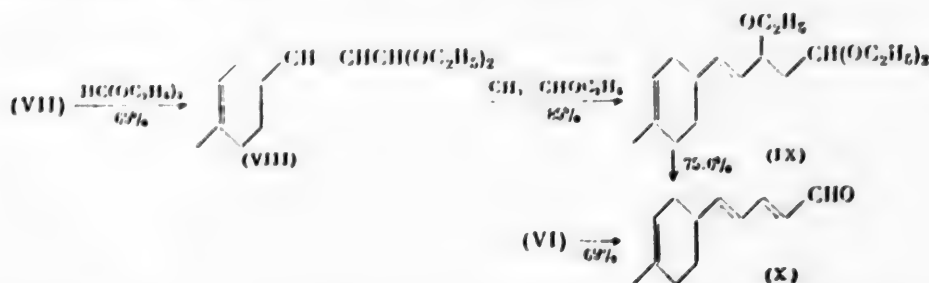


The condensation of the acetals (II) and (III) with vinyl ethers always formed a mixture of ether acetals, which were the products of the addition to the acetal of one, two, or more molecules of the vinyl ether. The amount of these secondary products depended on the experimental conditions and mainly on the ratio of the starting components. To obtain a high yield of the primary condensation product, it was necessary to use a large excess of the acetal. For example, under otherwise equal conditions, but with a threefold excess of the acetal (II) or (III), the yields of the ether acetals (IV) or (V) reached 37-40%. This is explained by the fact that both the starting acetals and the ether acetals formed as a result of the reaction reacted at almost the same rate with the vinyl ethers, and therefore excess of the acetals caused a decrease in the amount of products from further condensation [3, 7, 8, 10, 11]. However, even with a threefold excess of the starting acetal (II), in addition to the ether acetal (IV), we were able to isolate a 3% yield of the product (VI), which was formed as a result of the addition of two molecules of vinyl ethyl ether to the acetal (II) (higher-molecular compounds were not investigated).

When heated with a mixture of sodium acetate and acetic acid [9], the ether acetals (IV) and (V) were converted into a mixture of stereoisomeric  $\alpha, \beta$ -unsaturated aldehydes (VII), from which two isomers were isolated as the 2,4-dinitrophenylhydrazones and semicarbazones (Table 3).



On the basis of the ultraviolet absorption spectra of the derivatives of these isomeric aldehydes (VII), it may be considered that hydrolysis of the ether acetals (IV) and (V) gave as the main product the cis-aldehyde (VIIa), whose crystalline derivatives had a lower absorption intensity at the same wavelength in comparison with the absorption intensity of derivatives of the isomeric aldehyde (VIIb), which was obtained in a small amount in the hydrolysis products and was apparently the trans-aldehyde (VIIb) (Figs. 1 and 2). It should be noted that cis-trans isomers were not detected in subsequent stages of the synthesis. The action of ethyl orthoformate and anhydrous alcohol on the aldehyde (VII) in the presence of 85% orthophosphoric acid gave a 69% yield of the acetal (VIII), which was then condensed with vinyl ether. The ether acetal (IX) was formed in 85% yield without the formation of by-products. This is explained by the fact that the rate of addition of vinyl ethers to  $\alpha, \beta$ -unsaturated acetals is considerable greater than the rate of their addition to the ether acetals formed or saturated acetals [3, 7, 8, 10, 11]. Hydrolysis of the ether acetal (IX) gave the aldehyde (X), which was also obtained by hydrolysis of the ether acetal (VI).



In the preparation of  $\alpha, \beta$ -unsaturated aldehydes by the given method, the acetal formation, condensation, and hydrolysis could be combined and the isolation and purification of the intermediate products eliminated.


Repetition of all the given stages of the synthesis with the aldehyde (X) led to the aldehyde (XIII) and then the aldehyde (XVI), which is an analog of vitamin A aldehyde. These aldehydes were thick, yellow-green liquids, which changed rapidly during storage.





TABLE 1

## Aldehyde Acetals

Compound	Formula 	Reaction conditions						Boiling point (pressure in mm)	n <sub>D</sub> <sup>20</sup>	d <sub>4</sub> <sup>20</sup>	M/H		Found %		Calculated %	
		aldehyde (g)	HCl(OAc,H <sub>2</sub> ) (g)	anhydrous ethanol (ml)	% H <sub>3</sub> PO <sub>4</sub> (ml)	time (hr)	treatment method				found	calculated	C	H	C	H
(II)	RCH(OAc)H <sub>2</sub>	24.8	41.6*	6	0.40	8	A	101—103 (11)**	1.4558	0.8608	76.86	76.75	75.52	11.90	75.51	11.81
(III)	RCH(OAc)H <sub>2</sub>	44.0	—	255***	1.00****	48	B	117—118 (2)	1.4560	0.8948	76.86	76.75	75.52	11.90	75.51	11.81
(VIII)	RCH=CHCH(OAc)H <sub>2</sub>	45.0	50.0	18	1.10	24	B	102—103 (2)	1.4664	0.9197	67.59	67.00	74.91	11.05	74.93	10.78
(XIII)	RCH=CHCH(OAc)H <sub>2</sub>	14.2	14.0	10	0.36	24	B	126—127 (2)	1.4662	0.9380	77.90	75.77	76.41	10.54	76.75	10.47
(XIV)	RCH=CHCH(OAc)H <sub>2</sub>	6.1	4.3	6	0.40	24	B	170—172 (2)	1.5205	0.9450	80.29	84.54	78.10	10.28	78.22	10.21

\* Tetraethoxysilane instead of orthoformic ester.

\*\* According to literature data [13]: b. p. 100–102° (10 mm), n<sub>D</sub><sup>20</sup> 1.4552.

\*\*\* n-Butanol instead of ethanol.

\*\*\*\* HCl (d 1.21) instead of H<sub>3</sub>PO<sub>4</sub>.

## EXPERIMENTAL

The diethyl acetal of 4-methyl- $\Delta^3$ -tetrahydrobenzaldehyde (II) was obtained with the aid of tetraethoxysilane. After the reaction mixture had been kept for 8 hr, it was shaken for 0.5 hr with 30% alkali (525 ml of alkali per mole of tetraethoxysilane) to remove silicon compounds, and then the alcohol layer was separated, dried with potassium carbonate, and distilled (treatment method A).

The dibutyl acetal of 4-methyl- $\Delta^3$ -tetrahydrobenzaldehyde (III) was obtained by the addition of n-butanol and concentrated hydrochloric acid to the aldehyde (I). After the reaction mixture had been kept for a time, it was treated with pyridine (30 ml per mole of original aldehyde), then ether added and the ether layer washed with an ice-cooled 4% solution of sodium bicarbonate, dried over potassium carbonate, and vacuum distilled (treatment method B).

The acetals (VIII), (XI), and (XIV) were obtained in the following way. A mixture of the aldehyde (VI), (X), or (XIII), ethyl orthoformate, and anhydrous ethanol in the molar proportions of 1.0:1.1:3.0 and a catalytic amount of 85% orthophosphoric acid solution was left at room temperature for 24 hr. The reaction mixtures were then treated by method B.

The ratios of the components and the constants of the acetals (II), (III), (VIII), (XI), and (XIV) obtained and their yields are given in Table 1.

Condensation of acetals with vinyl ethers. Over a period of 1 hr, an equimolecular amount of the vinyl ether and a 10% solution of zinc chloride in ethyl acetate or butyl acetate [85 ml per mole of acetal, and in the case of acetal (II), 45 ml per mole of acetal] were added dropwise with stirring to the acetal (in some cases a three-fold excess of acetal was used) at 20–45°, while the temperature of the mixture was kept strictly within the given original range. The reaction mixture was then kept at this temperature for a further hour, cooled to room temperature, diluted with ether, and treated with dilute sodium hydroxide. The precipitate was removed and the ether layer dried over potassium carbonate and vacuum distilled. The ratios of the components, the reaction temperatures, and the constants of the ether acetals (IV), (V), (VI), (IX), (XII), and (XV) synthesized and their yields are given in Table 2.

TABLE 2


## Ether Acetals

Compound	Formula	Reaction conditions			Boiling point (pressure in mm)	$n_D^{20}$	$d_4^{20}$	MR		Found %			Calculated %		
		acetal (g)	vinyl ethyl ether (g)	reaction temperature (°C)	yield (%)			found	calcd.	C	H		C	H	
(IV)	$RCH(OC_2H_5)_2CH_2CH(OC_2H_5)_2$	96.5 (II)	36.0	70-75°	12.6	1.4580	0.9421	78.43	78.35	71.61, 71.50	1.38, 11.36		71.07	11.18	
(V)	$RCH(OC_2H_5)_2CH_2CH(OC_2H_5)_2$	50.8 (III)	20.0*	20-22	5.9	1.4570	0.9472	38.44	98.46	70.23, 70.10	1.20, 11.26		70.13	11.11	
(IX)	$RCH(OC_2H_5)_2CH_2CH(OC_2H_5)_2$	44.8 (VIII)	14.4	40-45	19.5	1.4563	0.9464	106.41	106.06	74.54, 74.30	2.15, 11.90		74.52	11.94	
(XII)	$RCH=CHCH(OC_2H_5)_2CH_2CH(OC_2H_5)_2$	17.7 (XI)	4.8	40-45	84.5	1.41-1.44 (3)	1.4616	87.63	87.12	72.58, 72.55	0.86, 10.68		72.97	10.81	
(XV)	$RCH=CHCH(OC_2H_5)_2CH_2CH(OC_2H_5)_2$	6.0 (XIV)	1.7	35-40	79.5	1.37-1.40 (0.2)	1.4664	98.63	98.39	74.75, 74.58	0.62, 10.48		74.49	10.63	

\* Vinyl butyl ether.

TABLE 3

## Aldehydes and Their Derivatives

Compound	Formula <div></div>	Yield (%)	Boiling point (pressure in mm)	n <sub>D</sub> <sup>20</sup>	2,4-Dinitrophenylhydrazones*				Semicarbazones**												
					melting point	found (%)		empirical formula	found %		ultraviolet ab- sorption spec- trum λ <sub>max</sub> (mμ)	melting point	found %		empirical formula	calcd. %		ultraviolet ab- sorption spectra λ <sub>max</sub> (mμ)			
						C	H		C	H			C	H		C	H				
(VIIa)- cis-	$\left. \begin{array}{l} RCH=CHCHO \\ RCH=CH_2CHO \\ R(CH=CH)_2CHO \\ R(CH=CH)_3CHO \end{array} \right\}$	65.0	89-93° (3)	1.500	180-181° 159-160	58.50 58.61 58.28 58.00	5.61 5.65 5.40 5.25	$C_{11}H_9O_4N_2$	58.18	5.45	377	2.55, 3.38	190-191° 175-176	63.80, 63.61 63.56 63.50	8.50, 8.32 8.12 8.31	$C_{11}H_9O_4N_2$	63.75	8.27	264	2.8 3.8	
(VIIb)- trans-									$C_{11}H_9O_4N_2$												
(X)			75.6	122-123 (3)	1.558	177-179	60.36 60.40	5.56 5.52	$C_{11}H_9O_4N_2$	60.67	5.66	387	3.90	191-192	67.06 67.18	8.2 8.21	$C_{11}H_9O_4N_2$	66.93	8.21	295	4.8
(XIII)			72.5	120-123 (0.2)	1.626	182-184**	62.55 62.58	5.86 5.98	$C_{11}H_9O_4N_2$	62.82	5.80	398	4.70	208-209.5	69.50 69.25	8.05 8.02	$C_{11}H_9O_4N_2$	69.47	8.16	323, 337	6.3 5.5
(XVI)	$R(CH=CH)_3CHO$				195-195.5***	54.35 64.82	6.02 5.87	$C_{11}H_9O_4N_2$	65.00	5.95	406	6.30									

\* Recrystallized from alcohol.

\*\* Recrystallized from methanol.

\*\*\* From acetone.

Hydrolysis of ether acetals to aldehydes. The ether acetals were hydrolyzed under standard conditions with identical ratios of reagents. A mixture of 73.0 g (0.27 mole) of the ether acetal (IV), 23.4 g of sodium acetate, and 247 ml of 95% acetic acid was stirred for 4 hr at 95-100° in a stream of nitrogen in the presence of hydroquinone. The reaction mixture was cooled and diluted with 600 ml of water, and the dark oil liberated was extracted with ligroin (b. p. 30-60°). The extract was washed with water, 4% sodium bicarbonate solution, and again with water and dried with sodium sulfate. Distillation in a stream of nitrogen yielded 25.7 g of a colorless liquid with b. p. 89-93° (3 mm),  $n_D^{20}$  1.500, which was a mixture of isomeric  $C_{10}$  aldehydes (VII).

Aldehyde (XVI). To 7.5 g of the unsaturated ether acetal (XIV) were added 15.6 ml of 95% acetic acid and 0.15 g of sodium acetate and the mixture stirred at 85-90° in a nitrogen atmosphere for 2 hr. After the normal treatment, the ligroin extract was treated with an alcohol solution of 3 g of 2,4-dinitrophenylhydrazine hydrochloride. Four recrystallizations of the precipitate from acetone yielded 2.9 g of the 2,4-dinitrophenylhydrazone of the aldehyde (XVI).

The constants of the aldehydes (VII), (X), (XIII), and (XVI) synthesized and their derivatives are given in Table 3.

Preparation of aldehydes (X) and (XIII) by the single-stage method (typical procedure). Over a period of 1 hr, 10 ml of vinyl ethyl ether and 10 ml of a 10% solution of zinc chloride in ethyl acetate were added to 30 g of undistilled acetal (VIII) at 40-45°. Stirring was continued for a further 2 hr at this temperature, and then 85 ml of 95% acetic acid and 8.0 g of sodium acetate were added, and the mixture was heated at 90-95° in a stream of nitrogen for 3 hr. Normal treatment and vacuum distillation yielded ~10-12 g of the aldehyde (X) with b. p. 120-123° (3 mm),  $n_D^{15}$  1.5584.

#### SUMMARY

1. It was shown that acetals of 4-methyl- $\Delta^3$ -tetrahydrobenzaldehyde condense with vinyl ethers to yield 12.6 to 19.5% of primary condensation products. Acetals of aldehydes with conjugated double bonds in the  $\alpha$ ,  $\beta$ -position in the side chain undergo this condensation much more readily, and the yield of the main reaction products is increased to 80-85%.

2. The condensation of the diethyl and dibutyl acetals of 4-methyl- $\Delta^3$ -tetrahydrobenzaldehyde and also 3-(4'-methylcyclohexen-3'-yl)-1,1-diethoxy-2-propene, 5-(4'-methylcyclohexen-3'-yl)-1,1-diethoxy-2,4-pentadiene, and 7-(4'-methylcyclohexen-3'-yl)-1,1-diethoxy-2,4,6-heptatriene with vinyl ethers yielded the corresponding ether acetals, which, by boiling with acetic acid, were converted smoothly into unsaturated aldehydes: 3-(4'-methylcyclohexen-3'-yl)-2-propen-1-al, 5-(4'-methylcyclohexen-3'-yl)-2,4-pentadien-1-al, 7-(4'-methylcyclohexen-3'-yl)-2,4,6-heptatrien-1-al, and 9-(4'-methylcyclohexen-3'-yl)-2,4,6,8-nonatetraen-1-al.

3. Hydrolysis of 3-(4'-methylcyclohexen-3'-yl)-1,1,3-triethoxy- and 3-(4'-methylcyclohexen-3'-yl)-1,1,3-tributoxypropane yielded two isomers, cis- and trans-3-(4'-methylcyclohexen-3'-yl)-2-propen-1-al.

4. From the ultraviolet absorption spectra of the 2,4-dinitrophenylhydrazones and semicarbazones of the  $\Delta^3$ -cyclohexene aldehydes we synthesized it was established that all the double bonds in the side chains were conjugated with the aldehyde group.

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# SYNTHESIS AND INVESTIGATION OF CYCLOALIPHATIC POLYENE COMPOUNDS

## II. SYNTHESIS OF POLYENE ACIDS AND ESTERS OF THE $\Delta^3$ -CYCLOHEXENE SERIES

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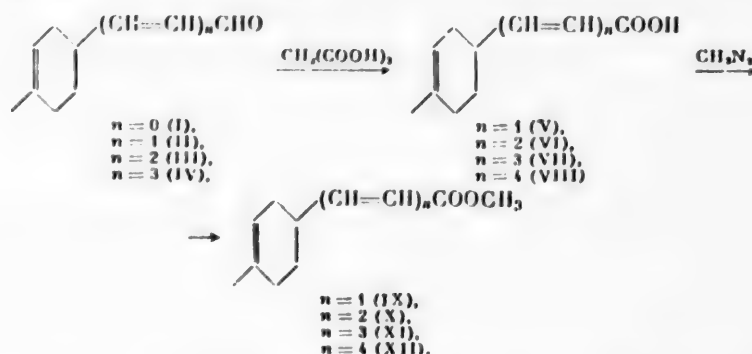
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Polyene aldehydes of the  $\Delta^3$ -cyclohexene series were synthesized in previous work [1]. In continuing these investigations, we studied the condensation of these aldehydes with malonic acid, which led to completely unknown polyene acids of the  $\Delta^3$ -cyclohexene series, and also synthesized the corresponding series of esters. On the basis of numerous literature data, it may be assumed that some of the compounds we synthesized will have biological activity.

The aldehydes (I-IV) were condensed with malonic acid in pyridine in the presence of small amounts of piperidine over the temperature range 20-110°.



For comparison of the reactivity of aldehydes containing multiple bonds conjugated with the carbonyl group, the above condensation was carried out under identical conditions with all the aldehydes. It was found that, as in the condensation of the  $\alpha, \beta$ -unsaturated acetals of these aldehydes with vinyl ethers [1], the presence of multiple bonds conjugated with the carbonyl group promoted the reaction. Thus, the acid (V) was obtained in 18% yield, while the acid (VI) was obtained in 63% yield.

The starting material for the preparation of the acid (VI) was a mixture of the isomeric aldehydes (II), whose structure we established in previous work [1]. As was expected, the acid (VI) was obtained in two forms, a crystalline and a liquid one, which again confirms the existence of cis and trans forms of the aldehyde (II). Structural isomers were not detected in the synthesis of the other acids.

When condensed with malonic acid under analogous conditions, the aldehydes (III) and (IV) gave many tarry products and very low yields of the acids (VII) and (VIII). Satisfactory yields of these acids (56-70%) were obtained only under milder condensation conditions.

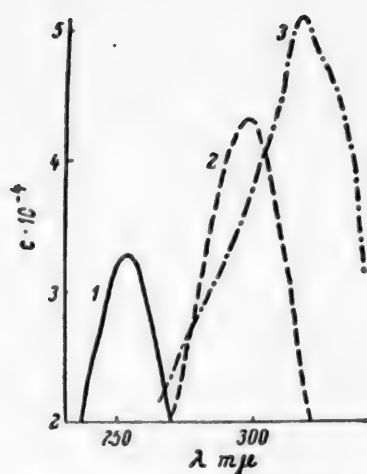


Fig. 1. Ultraviolet absorption spectra (in alcohol). 1) Acid (VI); 2) acid (VII); 3) acid (VIII).

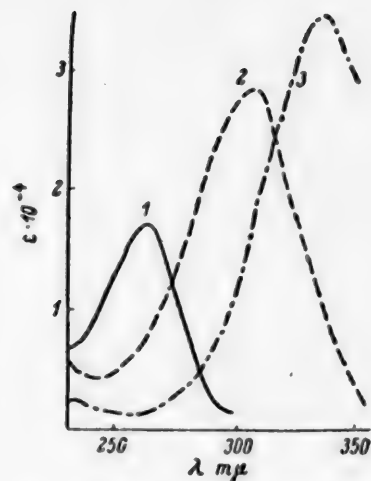


Fig. 2. Ultraviolet absorption spectra (in alcohol). 1) Ester (X); 2) ester (XI); 3) ester (XII).

TABLE 1

Substance		$\lambda_{\max}$ (m $\mu$ )	$\epsilon \cdot 10^{-4}$
Acid	(VI)	254	3.28
	(VII)	298	4.32
	(VIII)	320	5.10
Ester	(X)	264	1.67
	(XI)	304	2.82
	(XII)	338	3.45

We then prepared esters of the acids synthesized. From literature data [2] it is known that it is difficult to prepare methyl esters by the action of diazomethane on unsaturated acids without touching the double bonds. However, we were able to carry out this reaction successfully by using the calculated amount of diazomethane and reducing the temperature of the reaction mixture to  $-10$  to  $0^\circ$ ; all the acids then gave the corresponding methyl esters (IX-XII) in good yield. With the exception of the ester (XII), they were all thick, yellowish liquids with a weak odor and a specific gravity greater than 1, which distilled in vacuum without decomposition.

The acid (VII) and its methyl ester (XII) are analogs of vitamin A acid and ester.

The amides were prepared for characterization of the acids synthesized. The amides (XIII) and (XIV) were formed by the action of thionyl chloride in benzene on the acids (V) and (VI) with subsequent treatment with ammonia.

Attempts to prepare amides of the acids (VII) and (VIII) analogously and also by the reaction with oxalyl chloride were unsuccessful as the acids resinified during the preparation of the acid chlorides.

We plotted the ultraviolet absorption spectra of the acids and esters synthesized, and the data are given in Table 1 and Figs. 1 and 2. Many papers have been devoted to the study of ultraviolet absorption spectra of a polyene chain conjugated with a carboxyl group [3]. Acids containing one double bond conjugated with the carbonyl group are known to absorb in the region of 205 m $\mu$ . The absorption spectra of the acids (VI-VIII) and also their methyl esters (X-XII)\* agreed completely with the literature data for analogous polyene chains [3], and this confirms the structure of the compounds synthesized. The ultraviolet spectra of the acid (V) and its ester (IX) were not plotted.

#### EXPERIMENTAL

**3-(4'-Methylcyclohexen-3'-yl)-acrylic acid (V).** Into a 500-ml round-bottomed flask fitted with a reflux condenser were placed 45.6 g of malonic acid (dried at  $100^\circ$ ) dissolved in 96 ml of pyridine (dried over potassium hydroxide), 49.6 g of freshly distilled aldehyde (I) (b. p.  $72-73^\circ$  at 17 mm,  $n_D^{20}$  1.4738), and 1 ml of an-

\* The absorption spectra of alcohol solutions were plotted on an SF-4 spectrophotometer.



TABLE 2

Sub- stance	Found (%)		Empirical formula	Calculated %	
	C	H		C	H
(V)	72.17, 72.22	8.59, 8.51	C <sub>10</sub> H <sub>12</sub> O <sub>2</sub>	72.25	8.41
(XIII)	72.36, 72.68	9.33, 9.06	C <sub>10</sub> H <sub>15</sub> O <sub>2</sub> N	72.29	9.15
(IX)	73.11, 73.32	8.93, 8.85	C <sub>11</sub> H <sub>16</sub> O <sub>2</sub>	73.29	8.95
(VI)	75.02, 75.12	8.32, 8.50	C <sub>12</sub> H <sub>16</sub> O <sub>2</sub>	74.79	8.39
(XIV)	75.40, 75.49	8.73, 8.84	C <sub>12</sub> H <sub>17</sub> O <sub>2</sub> N	75.36	8.96
(X)	75.39, 75.58	8.90, 8.74	C <sub>13</sub> H <sub>18</sub> O <sub>2</sub>	75.68	8.79
(VII)	77.07, 76.81	8.48, 8.62	C <sub>14</sub> H <sub>18</sub> O <sub>2</sub>	77.02	8.31
(XI)	77.42, 77.63	8.70, 8.78	C <sub>15</sub> H <sub>20</sub> O <sub>2</sub>	77.55	8.68
(VIII)	78.61, 78.50	8.20, 8.20	C <sub>16</sub> H <sub>20</sub> O <sub>2</sub>	78.65	8.25
(XII)	79.00, 79.15	8.50, 8.57	C <sub>17</sub> H <sub>22</sub> O <sub>2</sub>	79.03	8.50

hydrous piperidine. The mixture was heated at 40-50° for 3 hr, and then the bath temperature was gradually raised to 100° at a rate such that the evolution of carbon dioxide was not too vigorous. The contents of the flask were then cooled to room temperature and poured into a 1-liter flask containing 70 ml of concentrated hydrochloric acid in 210 ml of water. The precipitated acid was collected and washed with several portions of very dilute acid. Three recrystallizations from a mixture of ethanol and water (4:1) yielded 10 g of 3-(4'-methylcyclohexen-3'-yl)-acrylic acid (V) with m. p. 108.5-109.5°.

Amide of 3-(4'-methylcyclohexen-3'-yl)-acrylic acid (XIII). A mixture of 1.0 g of the acid (V) in 20 ml of anhydrous benzene and 4 ml of SOCl<sub>2</sub> was boiled for 1 hr. After removal of the excess SOCl<sub>2</sub> in vacuum, the unpurified acid chloride was converted into the amide by treatment with 25% ammonia solution. We obtained 0.7 g of the amide (XIII) with m. p. 164.5-165.6° (in a sealed capillary) (from aqueous ethanol, 1:4).

Methyl 3-(4'-methylcyclohexen-3'-yl)-acrylate (IX). To a solution of 5 g of the crystalline acid (V) in 20 ml of absolute ether at -10 to 0° was added 300 ml of a dry ether solution of diazomethane obtained from 7.5 g of nitrosomethylurea and 34 ml of 50% potassium hydroxide and the mixture left overnight. Decomposition of the unreacted diazomethane with water and vacuum distillation yielded 4.8 g of the almost colorless ester (IX).

B. p. 94° (2 mm),  $n_D^{20}$  1.4930,  $d_4^{20}$  1.0054, MR 51.52; calc. 52.13.

5-(4'-Methylcyclohexen-3'-yl)-2,4-pentadienoic acid (VI). By the above procedure, from 23 g of the freshly distilled aldehyde (II) [b. p. 85-86° (2 mm),  $n_D^{17}$  1.5058] and 17 g of malonic acid in 36 ml of pyridine we obtained 21.8 g of the acid (VI) with m. p. 128-134° and also 5 g of a liquid acid, which crystallized when kept for a long period and was identical with the crystalline acid after recrystallization. Three recrystallizations from aqueous ethanol (1:4) yielded a total of 20.8 g of the acid (VI) with m. p. 136-138°.

The amide of the acid (XIV), which was obtained by the procedure described above, melted at 198.5-200.5° (in a sealed capillary) (from ethanol).

Methyl 5-(4'-methylcyclohexen-3'-yl)-2,4-pentadienoate (X). Treatment of 3.6 g of the acid (VI) with the calculated amount of diazomethane as described above gave 2.5 g of methyl 5-(4'-methylcyclohexen-3'-yl)-2,4-pentadienoate (X), which was yellow.

B. p. 140-141° (5 mm),  $n_D^{20}$  1.5220,  $d_4^{20}$  1.0337, MR<sub>D</sub> 60.85; calc. 60.29.

7-(4'-Methylcyclohexen-3'-yl)-2,4,6-heptatrienoic acid (VII). To a solution of 10 g of dried malonic acid in 24 ml of anhydrous pyridine was added 10 g of freshly distilled aldehyde (III) [b. p. 110-114° (0.2 mm)] and the mixture left for 3 days with protection from moisture. Then 6 drops of anhydrous piperidine was added and the mixture heated on a boiling water bath for 6 hr and finally at 120° for 0.5 hr. The normal treatment yielded 7 g of the acid (VII) with m. p. 143-154°. Four recrystallizations from aqueous alcohol (1:4) yielded 6 g of the acid (VII) with m. p. 160-162.5° (in a sealed capillary).

Methyl 7-(4'-methylcyclohexen-3'-yl)-2,4,6-heptatrienoate (XI). By the procedure described above, from 3 g of the acid (VII) and diazomethane we obtained 3.2 g of a product, which could not be distilled because of strong frothing due to the presence of tarry impurities. For isolation of the pure ester (XI), a solution

of the unpurified product in ligroin (b. p. 30-60°) was passed through a chromatography column of  $Al_2O_3$ . The methyl ester (XI) was eluted with ligroin first. Vacuum distillation yielded 2.5 g of yellow methyl ester.

B. p. 185-186° (3 mm),  $n_D^{20}$  1.5530,  $d_4^{20}$  1.0811,  $MR_D$  68.30; calc. 69.06.

9-(4'-Methylcyclohexen-3'-yl)-2,4,6,8-nonatetraenoic acid (VIII). A mixture of 5 g of malonic acid in 11 ml of anhydrous pyridine and 9 g of freshly distilled aldehyde (IV) [b. p. 137-140° (0.2 mm),  $n_D^{20}$  1.6260] was kept at room temperature for 3 days and then heated gradually as described above for the removal of  $CO_2$ . The normal treatment yielded 7.6 g of the acid (VIII) with m. p. 164-172°. Four recrystallizations from aqueous alcohol (1:4) yielded 6.8 g of the acid (VIII) with m. p. 173-176° (in a sealed capillary).

Methyl 9-(4'-methylcyclohexen-3'-yl)-2,4,6,8-nonatrienoate (XII). By the above procedure, from 1 g of the acid (VIII) and diazomethane we obtained 0.6 g of the methyl ester (XII) with m. p. 83-86° (from ethanol).

The analysis results for the substances obtained are given in Table 2.

#### SUMMARY

1. The condensation of  $\Delta^3$ -cyclohexene polyene aldehydes with malonic acid was studied. It was shown that the condensation was facilitated by an increase in the number of unsaturated bonds in the side chain conjugated with the aldehyde group.
2. A series of unsaturated acids of the  $\Delta^3$ -cyclohexene series was synthesized.
3. It was shown that the methyl esters of the unsaturated acids could be obtained without touching the double bonds by the action of the calculated amount of diazomethane at low temperatures.

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# SUBSTITUTED AND UNSUBSTITUTED 9-IMINO-10-VINYLA CRIDANS

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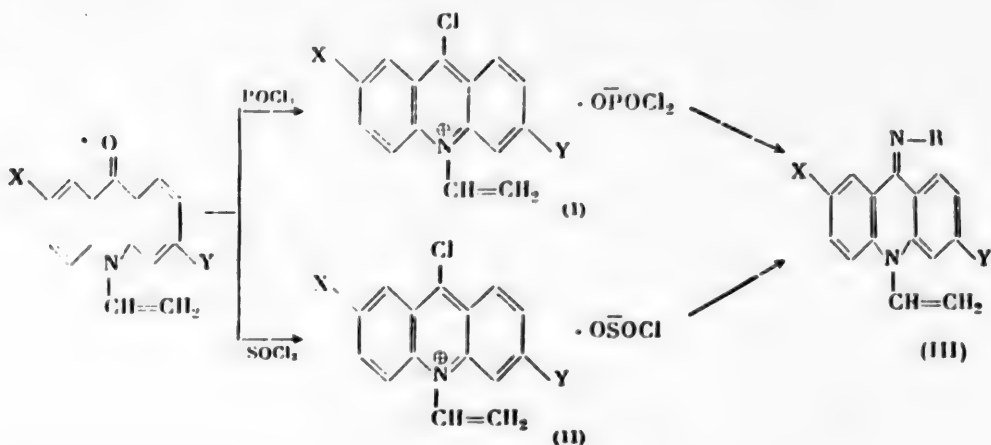
Acridine compounds are used widely in technology, medicine, and laboratory practice as dyes, antioxidants, anticorrosion agents, fluorescent indicators, drugs, etc.

We introduced a vinyl group into the acridine ring [1]. This made it possible to prepare a whole series of new acridine compounds capable of giving copolymers of high molecular weight with styrene, butadiene, isoprene, etc. [2-4].

In the present work, a description is given of the conversion of 10-vinylacridone and 3-chloro-7-methoxy-10-vinylacridone into dichlorophosphates and chlorosulfites by the action of phosphorus oxychloride and thionyl chloride, respectively, and the reactions of the 9-chloroacridinium salts obtained with amines.

The 9-chloroacridinium salts (I) and (II) have very labile chlorine atoms. When treated with water, they formed the corresponding acridones, and when treated with ammonia or primary amines, they formed 9-iminoacridans (III). The latter were readily crystallizable compounds with basic properties. In most cases their salts were unstable and readily hydrolyzed in aqueous solutions.

The free bases were capable of copolymerization with styrene and 1,3-dienes.



## EXPERIMENTAL

**9-Chloro-10-vinylacridinium dichlorophosphate (Ia).** A mixture of 20.3 g of 10-vinylacridone, 100 ml of anhydrous dichloroethane, and 13.4 ml of phosphorus oxychloride was boiled gently for 2 hr. The cooled

\*Deceased.

reaction mixture was poured into 500 ml of absolute ether. The precipitated yellow crystals were collected, washed with ether on the filter, and dried in a vacuum desiccator. The yield was 28 g (81.6%). The m. p. was  $\sim 190^\circ$  (decomp.). Aqueous solutions of compound (Ia) had a yellow color and a green-violet fluorescence. On standing, these solutions deposited 10-vinylacridone quite rapidly.

Found %: Cl\* 28.26.  $C_{15}H_{11}O_2NFCI_3$ . Calculated %: Cl 27.90.

9-Chloro-10-vinylacridinium chlorosulfite (IIa). A solution of 22 g of 10-vinylacridone in 100 ml of anhydrous dichloroethane was heated until it boiled gently, and then 17.7 g of thionyl chloride was added in small portions from a funnel through the reflux condenser. The mixture was boiled gently for 2 hr. The reaction mixture was then cooled to room temperature and the crystals collected, washed with absolute ether on the filter, and dried in a vacuum desiccator. We obtained 20 g (58.8%) of a substance with m. p.  $188^\circ$  (decomp.). The substance dissolved in water to form a yellow solution with a violet fluorescence, which very rapidly (instantaneously on heating) deposited 10-vinylacridone.

Found %: Cl 20.45; S 9.43.  $C_{15}H_{11}O_2NSCl_2$ . Calculated %: Cl 20.85; S 9.42.

3,9-Dichloro-7-methoxy-10-vinylacridinium dichlorophosphate (Ib). To a gently boiling solution of 28 g of 3-chloro-7-methoxy-10-vinylacridone in 400 ml of anhydrous dichloroethane was added 13 g of phosphorus oxychloride. The mixture was boiled gently for 1.5 hr, and orange crystals of (Ib) separated. After the reaction mixture had been cooled to room temperature, the crystals were collected, washed on the filter with absolute ether, and dried in a vacuum desiccator. The yield was 26 g (68.2%). The m. p. was  $196^\circ$  (decomp.). On standing, aqueous solutions of the substance deposited 3-chloro-7-methoxy-10-vinylacridone.

Found %: Cl 32.00.  $C_{16}H_{12}O_3NPCI_4$ . Calculated %: Cl 32.31.

3,9-Dichloro-7-methoxy-10-vinylacridinium chlorosulfite (IIb). By the method given for (Ia), from 28 g of 3-chloro-7-methoxy-10-vinylacridone in 400 ml of anhydrous dichloroethane and 17.7 g of thionyl chloride we obtained 20 g (50%) of a product with m. p.  $193^\circ$  (decomp.). Aqueous solutions of the substance had a green fluorescence. On standing, the solution deposited the corresponding acridone.

Found %: Cl 26.80; S 7.75.  $C_{16}H_{12}O_3NSCl_3$ . Calculated %: Cl 26.29; S 7.92.

9-Imino-10-vinylacridan (IIIa). A 37.4-g sample of the 9-dichlorophosphate (Ia) (or the corresponding amount of the chlorosulfite, though the yield of the final product was better with the dichlorophosphate) was dissolved in 500 ml of water. The solution was filtered rapidly and excess 5% aqueous ammonia solution added. Fine red crystals then separated, and these were coagulated by heating the reaction mixture. The precipitate was collected, washed with water on the filter, dried, and recrystallized from aqueous alcohol. The yield was 15 g (68.1%). The m. p. was  $168-169^\circ$ . The coarse red crystals were readily soluble in dichloroethane, alcohol, dioxane, hot benzene, and other organic solvents.

Found %: N 12.56.  $C_{15}H_{12}N_2$ . Calculated %: N 12.73.

Mixing alcohol solutions of 9-imino-10-vinylacridan and picric acid precipitated brick red crystals of the picrate with m. p.  $212^\circ$ .

3-Phenylimino-10-vinylacridan (IIIb). Mixing a solution of 37.4 g of dichlorophosphate (Ia) in 500 ml of water and 200 ml of an 8% aqueous alcohol solution of aniline precipitated light orange leaflets of 3-phenylimino-10-vinylacridan. The yield was 23 g (77.4%). The m. p. was  $148-149^\circ$  (from alcohol). The substance was soluble in alcohol, ether, benzene, and other organic solvents.

Found %: N 9.48.  $C_{21}H_{16}N_2$ . Calculated %: N 9.46.

The picrate formed red crystals with m. p.  $190-193^\circ$ .

9-p-Methoxyphenylimino-10-vinylacridan (IIIc). By the method described in the previous section, from 37.4 g of the dichlorophosphate (Ia) in 500 ml of water and 150 ml of a 15% alcohol solution of p-anisidine we obtained 17.1 g (60%) of the substance. It formed orange crystals (from alcohol + ether).

Found %: N 8.22.  $C_{22}H_{18}ON_2$ . Calculated %: N 8.55.

\* The total chlorine content was determined by the method described in previous work [2, 3].

3-Chloro-7-methoxy-10-vinyl-9-iminoacridan (III<sub>d</sub>). From 43.8 g of the dichlorophosphate (Ib) in 600 ml of water and a 15% aqueous solution of ammonia we obtained 25 g (88%) of the substance as bright red crystals with m. p. 199-200° (from alcohol + ether). The substance was readily soluble in alcohol, acetone, and benzene and less soluble in dichloroethane and chloroform.

If an aqueous solution of the acridinium salt was added to excess of a 25% ammonia solution the iminoacridan precipitated as yellow crystals with the same melting point.

Found %: N 9.30.  $C_{16}H_{13}ON_2Cl$ . Calculated %: N 9.62.

The picrate had m. p. 251-252°.

3-Chloro-7-methoxy-9-phenylimino-10-vinylacridan (III<sub>e</sub>). From 43.8 g of the dichlorophosphate (Ib) in 500 ml of water and 18 g of aniline in 1000 ml of aqueous alcohol we obtained 28 g (77.7%) of the compound (III<sub>e</sub>) as orange-red crystals with m. p. 145-146° (from alcohol + ether). Solutions of the acridan (III<sub>e</sub>) in ether were yellow, and in benzene, chloroform, and dichloroethane, red.

Found %: N 7.77.  $C_{22}H_{17}ON_2Cl$ . Calculated %: N 7.77.

The picrate formed orange-red crystals with m. p. 183-184°.

3-Chloro-7-methoxy-9-p-methoxyphenylimino-10-vinylacridan (III<sub>f</sub>). From a mixture of 43.8 g of the dichlorophosphate (Ib) in 500 ml of water and 24.6 g of p-anisidine in 300 ml of alcohol, which was heated for 30 min, we obtained 22 g (53%) of the acridan (III<sub>f</sub>) as brown crystals with m. p. 132-133° (from ether). The substance was soluble in alcohol, chloroform, ether, and benzene.

Found %: N 7.24.  $C_{23}H_{19}O_2N_2Cl$ . Calculated %: N 7.17.

The picrate formed yellow crystals with m. p. 150°.

#### SUMMARY

1. The action of phosphorus oxychloride and thionyl chloride on 10-vinylacridones yielded 9-chloro-10-vinylacridinium and 3,9-dichloro-7-methoxy-10-vinylacridinium dichlorophosphates and chlorosulfites.

2. It was shown that treatment of 9-chloro-10-vinylacridinium dichlorophosphates and chlorosulfites with ammonia and amines gives 9-imino-10-vinylacridan and its derivatives.

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## STERIC HINDRANCE IN MOLECULES OF 2-ARYLBENZTHIAZOLES

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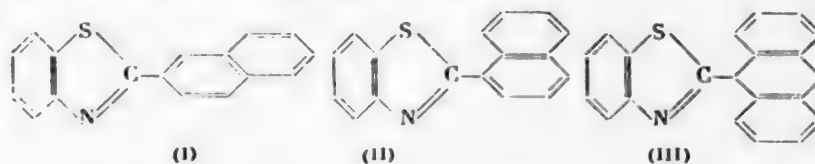
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November, 1960

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Steric hindrance in quaternary salts of 2-aryl derivatives of nitrogen heterocyclic compounds was considered in previous articles [1, 2]. As a result of disruption of the coplanarity of the nuclei, the quaternary salts absorb less intensely and at shorter wavelengths than the corresponding sulfates.

In the present work we studied the light absorption of alcohol solutions of 2- $\alpha$ -naphthylbenzthiazole (I), 2- $\beta$ -naphthylbenzthiazole (II), and 2-(9'-anthryl)-benzthiazole (III),



and also the light absorption of their sulfates and methiodides or methoperchlorates. It might have been expected that the steric hindrance would increase from compound (I) to (III), and in the molecules of compounds (II) and (III) the nuclei would be noncoplanar not only in the quaternary salts, but also in the sulfates and possibly in the free bases. A study of the absorption spectra confirmed these hypotheses.

With respect to the steric interaction of the naphthalene and thiazole nuclei, the molecule of 2- $\beta$ -naphthylbenzthiazole does not differ substantially from the molecule of 2-phenylbenzthiazole. Therefore, as in the case of 2-phenylbenzthiazole and its salts [2], as a result of disruption of the coplanarity of the aryl and thiazole rings, the absorption band of 2- $\beta$ -naphthylbenzthiazole methiodide (Ib) is less intense and hypsochromically displaced in comparison with the absorption bands of the sulfate (Ia), in whose molecule the nuclei are coplanar. The free base (I) differs little from the sulfate as regards absorption intensity (Fig. 1).

Completely different relations are observed on the absorption curves of 2- $\alpha$ -naphthylbenzthiazole (II), its sulfate (IIa), and its methiodide (IIb) (Fig. 2).

All three bands lie almost parallel and their intensities are low. This means that the coplanarity of the nuclei is disrupted both in the molecules of the quaternary salt and sulfate and in the molecule of the free base. This may be observed even more clearly in Fig. 3, which shows absorption curves of 2-(9'-anthryl)-benzthiazole (III) and its salts, the sulfate (IIIa) and the methoperchlorate (IIIb). Here the absorption curves of the two salts merge almost completely. The absorption curve of the free base differs from them only in a more strongly expressed fine structure, which is inappreciable with the salts because of solvation, and somewhat less intense absorption in the region of 270-300 m $\mu$ .

Despite the very strong disruption of coplanarity, there is still some conjugation between the anthracene and benzthiazole nuclei. As Fig. 4 shows, the absorption curves of 2-(9'-anthryl)-benzthiazole (III) and an equimolecular mixture of anthracene and 2-methylbenzthiazole (IIIc) almost coincide in intensity, but the absorption maxima of the first curve are appreciably displaced bathochromically.



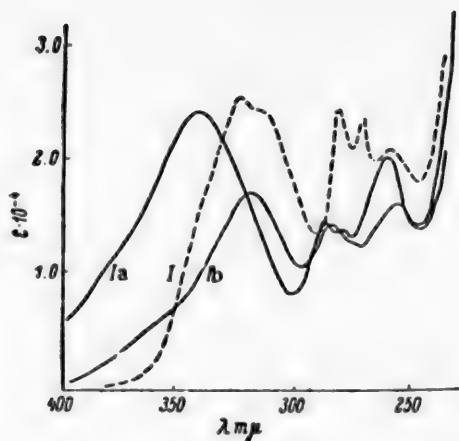


Fig. 1. Absorption spectra of alcohol solutions: I) 2-B-naphthylbenzthiazole; Ia) 2-B-naphthylbenzthiazole sulfate; Ib) 2-B-naphthylbenzthiazole methiodide.

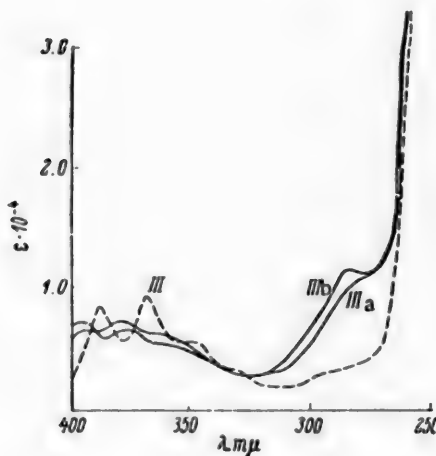


Fig. 3. Absorption spectra of alcohol solutions: III) 2-(9'-anthryl)-benzthiazole; IIIa) 2-(9'-anthryl)-benzthiazole sulfate; IIIb) 2-(9'-anthryl)-benzthiazole methoperchlorate.

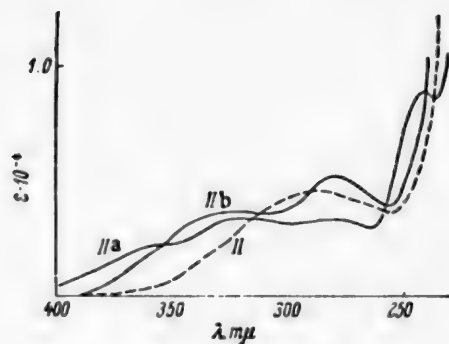
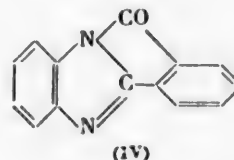


Fig. 2. Absorption spectra of alcohol solutions: II) 2- $\alpha$ -naphthylbenzthiazole; IIa) 2- $\alpha$ -naphthylbenzthiazole sulfate; IIb) 2- $\alpha$ -naphthylbenzthiazole methiodide.

Among the derivatives of 2-phenylbenzimidazole, there is the simple possibility of holding the phenyl group in the plane of the imidazole by means of a carbonyl group. The absorption curves of the sulfate (IVa) and methoperchlorate (IVb) of o-benzoyl-ene-2,1-benzimidazole (IV),



in contrast to the corresponding salts of 2-arylbenzimidazoles [2], differ very little, as is shown by Fig. 5.

#### EXPERIMENTAL\*

**2-B-Naphthylbenzthiazole.** A mixture of 1.3 g of o-aminothiophenol and 2 g of  $\beta$ -naphthoyl chloride [3] was heated carefully until a vigorous reaction began. The tube was cooled and then heated again for a few minutes in a metal block at 160° to remove water vapor and hydrogen chloride. The cooled product was ground with sodium hydroxide, dried, and recrystallized

from methanol (50 ml). The pale yellow platelets had m. p. 129.5°. The yield was 0.8 g. About another gram of crude material was isolated from the mother solution.

$\lambda_{\max}^{\bullet}$  324 (2.52), 282 (2.44), 271 (2.34), 258 (2.10) m $\mu$ ;  $\lambda_{\min}$  290 (1.36), 275 (2.10), 265 (1.98), 246 (2.00) m $\mu$ .

Found %: N 5.47, 5.33.  $C_{17}H_{11}NS$ . Calculated %: N 5.36.

**Sulfate:**  $\lambda_{\max}$  342 (2.40), 288 (1.46), 279 (2.40), 260 (2.00) m $\mu$ ;  $\lambda_{\min}$  301 (0.82), 283 (1.36), 275 (1.32), 246 (1.40) m $\mu$ .

\* The melting point are corrected.

\*\* The molecular extinctions  $\times 10^{-4}$  are given in parentheses. All spectral measurements were made on a SF-4 spectrophotometer.

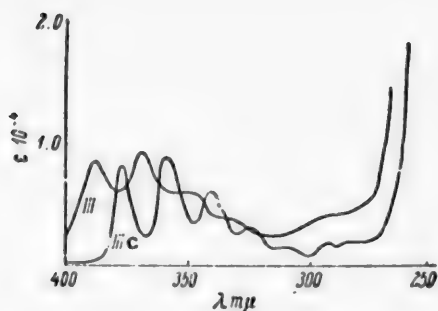


Fig. 4. Absorption spectra of alcohol solutions: III) 2-(9'-anthryl)-benzthiazole; IIIc) equimolecular mixture of anthracene and 2-methylbenzthiazole.

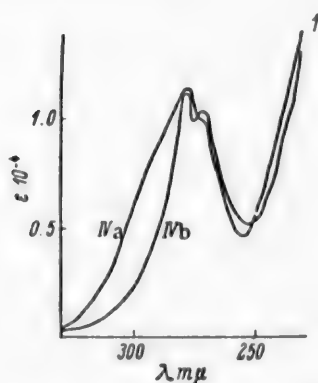


Fig. 5. Absorption curves of alcohol solutions: IVa) o-benzoylene-2,1-benzimidazole sulfate; IVb) o-benzoylene-2,1-benzimidazole perchlorate.

**2-(9'-Anthryl)-benzthiazole.** A mixture of 0.67 g of o-aminothiophenol and 1.1 g of 9-anthraldehyde [5] was heated at 130-140° for ~1 hr and then for 5 min at 170° until the water had been removed completely. The product was recrystallized from ethyl acetate. The dark yellow needles had m. p. 212-213.5°; the yield was 0.51 g (31%).  $\lambda_{\max}$  387 (0.86), 368 (0.94), 255 (11.10) mμ;  $\lambda_{\min}$  378 (0.58), 315 (0.18) mμ.

Found %: S 10.14, 10.30.  $C_{21}H_{13}NS$ . Calculated %: S 10.29.

Sulfate:  $\lambda_{\max}$  393 (0.66), 376 (0.66), 253 (9.60) mμ;  $\lambda_{\min}$  385 (0.58) mμ.

**The methoperchlorate** was obtained by heating a mixture of 0.35 g of the base and 0.25 g of dimethyl sulfate on a water bath for 2 hr. The methoperchlorate was precipitated from an aqueous solution of the salt obtained with sodium perchlorate. The yield of crude product was 0.36 g. After recrystallization from methanol, the fine crystals had decomp. p. 276°.  $\lambda_{\max}$  395 (0.72), 378 (0.74), 284 (1.15), 253 (10.70) mμ;  $\lambda_{\min}$  388 (0.64), 325 (0.26), 275 (1.10) mμ.

Found %: Cl 8.18, 8.10.  $C_{22}H_{16}O_4NSCl$ . Calculated %: Cl 8.34.

**o-Benzoylene-2,1-benzimidazole [6].** A mixture of 5.4 g of o-phenylenediamine and 7.4 g of phthalic anhydride was heated at 125-130° until the evolution of water vapor ceased. The melt was ground and recrystallized twice from acetic anhydride. The yellow needles had m. p. 210° and the yield was 4.5 g.  $\lambda_{\max}$  338 (0.60), 300 (0.63), 288 (0.83), 271 (4.20), 237 (2.60) mμ;  $\lambda_{\min}$  310 (0.33), 295 (0.66), 283 (0.70), 248 (1.66), 216 (1.60) mμ.

The methiodide was obtained by heating a mixture of the base and dimethyl sulfate on a water bath for 45 min and precipitation with potassium iodide from an aqueous solution of the salt obtained. Recrystallization from methanol gave light yellow platelets with m. p. 203-203.5° (decomp.).  $\lambda_{\max}$  319 (1.70), 235 (1.44), 255 (1.62) mμ;  $\lambda_{\min}$  297 (1.06), 271 (1.22), 245 (1.40) mμ.

Found %: I 31.28, 31.45.  $C_{18}H_{14}NSI$ . Calculated %: I 31.51.

**2- $\alpha$ -Naphthylbenzthiazole.** A 5-g sample of o-aminothiophenol was mixed with 6.5 g of  $\alpha$ -naphthaldehyde [4]. Heat was evolved during mixing and a solid was formed on cooling. The mixture was heated at 150° for ~1 hr until the evolution of water ceased. A light yellow semisolid mass was obtained. The substance was recrystallized from alcohol (100 ml). We obtained 4 g of platelets with m. p. 127°.  $\lambda_{\max}$  286 (0.46), 225 (3.80) mμ;  $\lambda_{\min}$  256 (0.37) mμ.

Found %: N 5.57, 5.42.  $C_{17}H_{11}NS$ . Calculated %: N 5.36.

Sulfate:  $\lambda_{\max}$  320 (0.34), 284 (0.33), 240 (0.88), 215 (2.14) mμ.

The methiodide was obtained by heating a mixture of the base and dimethyl sulfate in a sealed tube on a water bath for 3 hr. The aqueous solution of the salt obtained was treated with ether and the product precipitated with potassium iodide. After recrystallization from alcohol, the light yellow crystals had m. p. 204.5° (decomp.).  $\lambda_{\max}$  281 (0.52), 225 (12.30) mμ;  $\lambda_{\min}$  257 (0.38) mμ.

Found %: I 31.33, 31.42.  $C_{18}H_{14}NSI$ . Calculated %: I 31.51.

Sulfate:  $\lambda_{\max}$  278 (1.14)  $\mu\mu$ ;  $\lambda_{\min}$  255 (0.48)  $\mu\mu$ .

The methoperchlorate was obtained by heating a mixture of 1.1 g of the base and 0.7 g of dimethyl sulfate at 120° for 15-20 min. The melt obtained was dissolved in water, the solution filtered, and a saturated solution of sodium perchlorate added to the filtrate. On standing for a day, the precipitated oil solidified. The yield was 0.7 g. The substance was recrystallized from nitrobenzene. The fine, colorless crystals were readily soluble in alcohol and acetone and had m. p. 178°.  $\lambda_{\max}$  278 (1.11), 272 (1.04)  $\mu\mu$ ;  $\lambda_{\min}$  276 (1.00), 253 (0.51)  $\mu\mu$ .

Found %: N 8.51, 8.57.  $C_{15}H_{11}O_5N_2Cl$ . Calculated %: N 8.37.

#### SUMMARY

The absorption spectra of alcohol solutions of 2- $\beta$ -naphthylbenzthiazole, 2- $\alpha$ -naphthylbenzthiazole, 2-(9'-anthryl)-benzthiazole, and o-benzoylene-2,1-benzimidazole were determined. From a comparison of the absorption curves it was concluded that in quaternary salts of 2- $\beta$ -naphthylbenzthiazole, in quaternary and simple salts of 2- $\alpha$ -naphthylbenzthiazole and 2-(9'-anthryl)-benzthiazole, and also in the molecules themselves of the last two bases the nuclei are noncoplanar. The nuclei are held in one plane in the molecule of o-benzoylene-2,1-benzimidazole, and therefore the absorption curves of its methoperchlorate and sulfate are very similar.

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## REACTION OF BENZENESULFONYL CHLORIDE WITH ALCOHOLS

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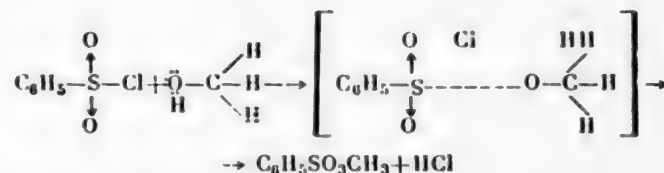
November, 1960

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Until now, investigators studying the hydrolysis and alcoholysis of sulfonyl chlorides have paid most attention to the relation of these processes to the structure of the sulfonyl chloride. For example, the relation of the reaction rate to the nature of the substituents in the nucleus has been studied among derivatives of benzenesulfonyl chloride [1]. However, the effect of the structure of the alcohol on alcoholysis has been studied superficially and only on a limited number of examples [2] or the study has been of a purely quantitative nature for preparative purposes [3].

The comparative quantitative characteristics of alcoholysis of sulfonyl chlorides by alcohols of various structures is therefore of definite interest. Hydrolysis and alcoholysis in excess water or alcohol are pseudomonomolecular processes [1,2]. With equimolecular amounts of water and sulfonyl chloride, the hydrolysis at 20 and 40° is a second order reaction (Table 3), while alcoholysis is complicated by the simultaneous formation of alkyl chlorides and ethers [3]. However, it was found that (under conditions where the process is slow and the degree of reaction is low) at 0° and in the presence of a sensitive control, it is possible to follow alcoholysis without the complication of other processes. In this case, the constants can be calculated for any order because of the low degree of conversion occurring over a relatively long time. However, there are no grounds for doubting that alcoholysis, like hydrolysis, is a second order reaction, as the process is strictly pseudomonomolecular when there is excess of one of the components. The rate constants of alcoholysis, calculated for a second order process (Table 1), decreased regularly with an increase in the number of carbon atoms in the chain of normal primary alcohols from methyl to nonyl alcohol. A decrease in the constants occurred with the successive replacement of hydrogens of the methyl groups of ethanol and methanol by phenyl and p-nitrophenyl groups.

The observed changes in the rate constants of benzenesulfonyl chloride alcoholysis by various alcohols and phenols appear to be a rule and are apparently caused by the different nucleophilicity of the oxygen of the hydroxyl group, which may indicate a nucleophilic mechanism for the replacement of chlorine at the sulfur in a sulfonyl chloride ( $S_N2$ ).



The relatively high reactivity of p-chlorophenol, which is close to that of ethanol, is apparently caused by the positive tautomeric effect (+T) of chlorine, which produces quite a high electron density at the oxygen at the moment of reaction.

As regards nucleophilic properties, the different nitro derivatives of phenol should lie in an order that is the reverse of the order of their acidity (Table 2).

TABLE 1

Water, alcohol, or phenol	$K_1 = \frac{x}{IA(A-x)}$	Relative reactivity
H <sub>2</sub> O	$6.45 \cdot 10^{-6}$	1.2200
CH <sub>3</sub> OH	$5.25 \cdot 10^{-6}$	1.0000
C <sub>2</sub> H <sub>5</sub> OH	$1.62 \cdot 10^{-6}$	0.3120
n-C <sub>4</sub> H <sub>9</sub> OH	$6.54 \cdot 10^{-7}$	0.1250
n-C <sub>5</sub> H <sub>11</sub> OH	$6.03 \cdot 10^{-7}$	0.1150
n-C <sub>9</sub> H <sub>19</sub> OH	$3.72 \cdot 10^{-7}$	0.0708
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CH <sub>2</sub> OH	$3.24 \cdot 10^{-7}$	0.0630
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> OH	$1.91 \cdot 10^{-7}$	0.0364
p-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH	$5.55 \cdot 10^{-8}$	0.0106
4-Chlorophenol	$1.25 \cdot 10^{-6}$	0.2380
Phenol	$3.34 \cdot 10^{-7}$	0.0636
2-Nitrophenol	$1.32 \cdot 10^{-7}$	0.0251
4-Nitrophenol	$9.75 \cdot 10^{-8}$	0.0186
2,4-Dinitrophenol	$6.57 \cdot 10^{-8}$	0.0125

TABLE 2

Acid	pK (electrolytic dissociation)
2,4-Dinitrophenol	3.96
4-Nitrophenol	7.15
2-Nitrophenol	7.17
Phenol	9.89

TABLE 3

## Hydrolysis of Benzenesulfonyl Chloride

Time (min)	20°			40°		
	R (ohm)	mole	$K_1 \cdot 10^3$	R (ohm)	mole	$K_1 \cdot 10^3$
0	0	0	0	0	0	0
15	4000	0.033	2.28	5600	0.080	6.30
30	3600	0.060	2.13	4000	0.150	6.47
45	3000	0.089	2.16	3200	0.185	6.18
75	2600	0.140	2.25	2800	0.260	6.82
105	1200	0.190	2.24	2300	0.310	6.20
135	1000	0.230	2.21	2000	0.350	6.13
195	800	0.290	2.10	1500	0.420	6.42
285	650	0.370	2.05	1000	0.490	6.62

However, while the degree of acidity of o- and p-nitrophenols is practically the same, their nucleophilicities are different. This must be ascribed to the so-called "ortho effect," which, in the given case, is by a hydrogen bond, which is a factor that considerably increases the electron density on the oxygen of the hydroxyl group.

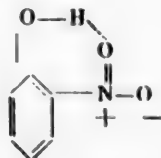
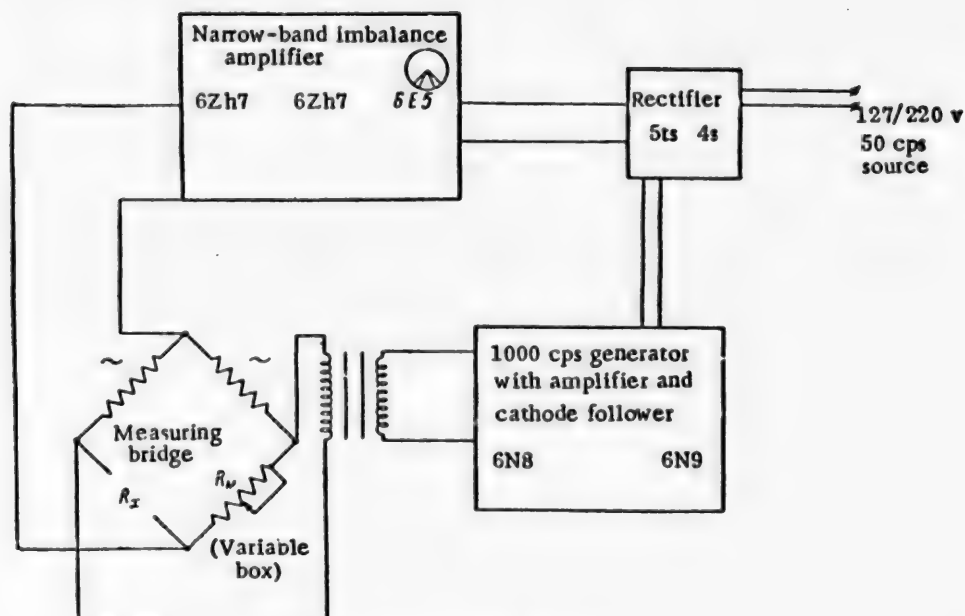


TABLE 4  
Alcoholysis of Benzenesulfonyl Chloride

Time (min)	H <sub>2</sub> O		CH <sub>3</sub> OH		C <sub>2</sub> H <sub>5</sub> OH		n-C <sub>4</sub> H <sub>9</sub> OH		n-C <sub>6</sub> H <sub>13</sub> OH		C <sub>8</sub> H <sub>17</sub> CH <sub>2</sub> OH		C <sub>10</sub> H <sub>21</sub> OH		p-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> OH	
	R (thousand ohms)	X (mole · 10 <sup>-3</sup> )	R (thousand ohms)	X (mole · 10 <sup>-3</sup> )	R (thousand ohms)	X (mole · 10 <sup>-3</sup> )	R (thousand ohms)	X (mole · 10 <sup>-3</sup> )	R (thousand ohms)	X (mole · 10 <sup>-3</sup> )	R (thousand ohms)	X (mole · 10 <sup>-3</sup> )	R (thousand ohms)	X (mole · 10 <sup>-3</sup> )	R (thousand ohms)	X (mole · 10 <sup>-3</sup> )
15	60.00	0.10000	182.00	0.02501	99.60	0.01001	85.00	0.00710	99.60	0.00551	130.00	0.00501	199.90	0.00301	138.80	0.00081
30	58.20	0.19040	180.50	0.05020	99.40	0.02000	83.00	0.01901	99.40	0.02201	128.00	0.01930	199.30	0.01151	137.50	0.00320
45	57.40	0.27040	179.00	0.07510	99.25	0.02902	80.00	0.04431	99.15	0.04502	127.60	0.03701	199.00	0.02301	135.00	0.00590
60	57.00	0.50000	170.00	0.13001	99.00	0.05103	75.60	0.08010	99.00	0.06510	113.80	0.08012	198.70	0.03501	133.50	0.00820
75	54.80	0.70000														
105																
120																
135																
145																
185	47.00	1.25000	158.00	0.29000	98.95	0.12010	71.50	0.12001	98.95	0.11000			197.90	0.05203	131.30	0.01600
235	42.00	1.80000	143.30	0.43001	98.60	0.18003	67.50	0.17013	98.60	0.11000						
285																
$k_s$	8.45 · 10 <sup>-6</sup>	5.25 · 10 <sup>-6</sup>	1.62 · 10 <sup>-6</sup>	6.54 · 10 <sup>-7</sup>	6.03 · 10 <sup>-7</sup>	3.72 · 10 <sup>-7</sup>	3.24 · 10 <sup>-7</sup>	1.91 · 10 <sup>-7</sup>	5.55 · 10 <sup>-8</sup>							





Block plan of MM 34-53.

TABLE 5

Phenols

Time (min)	4-Chlorophenol		Phenol		2-Nitrophenol		4-Nitrophenol		2,4-Dinitrophenol	
	R (thousand ohms)	X (mole $\cdot 10^{-3}$ )	R (thousand ohms)	X (mole $\cdot 10^{-3}$ )	R (thousand ohms)	X (mole $\cdot 10^{-3}$ )	R (thousand ohms)	X (mole $\cdot 10^{-3}$ )	R (thousand ohms)	X (mole $\cdot 10^{-3}$ )
15	54.40	0.02000	158.00	0.00503	67.80	0.00201	31.93	0.00152	42.65	0.00104
30	54.35	0.03600	157.00	0.01013						
45	54.00	0.06010			67.60	0.00590	31.90	0.00431	42.58	0.00310
60			156.00	0.02012						
75	53.50	0.09103							42.50	0.00512
105	52.60	0.14031			67.55	0.01401	31.88	0.01002		
120			155.00	0.04011						
135									42.40	0.00851
165							31.85	0.01601		
185			154.00	0.06030						
195					67.45	0.02580			42.30	0.01301
235	51.40	0.28005					31.84	0.02203		
285	50.00	0.35010	134.00	0.09510	67.30	0.03801	31.81	0.02813	42.20	0.01803
$K_s$	$1.25 \cdot 10^{-6}$		$3.31 \cdot 10^{-7}$		$1.32 \cdot 10^{-7}$		$9.75 \cdot 10^{-8}$		$6.57 \cdot 10^{-8}$	

Thus, the  $S_N2$  mechanism for the reaction of benzenesulfonyl chloride with alcohols and phenols is adequately substantiated, and the rate constants may be used as a quantitative comparative characteristic of the nucleophilic properties of alcohols and phenols in this reaction.

The relative reactivity of the hydroxyl-containing compounds studied may be represented clearly if the rate constant for the alcoholysis of benzenesulfonyl chloride by methanol is taken as unity (Table 1). Attention is attracted by the sharp fall in the activity of normal primary aliphatic alcohols from methanol to butanol with a subsequent slow decrease as the hydrocarbon chain is lengthened and the considerable activity of p-chlorophenol.

## EXPERIMENTAL

In the work we used carefully purified compounds with boiling or melting points corresponding to literature data. The moisture content (by Fischer's method) of the acetone lay in the range of 0.04-0.05%, and that of the alcohols varied over the range of 0.17-0.25%.

For the electrometric measurements, we used a sonic frequency box bridge with an electronic optical indicator of the type MM 34-53, which was constructed by our co-workers in the Leningrad Chemcopharmaceutical Institute, V. M. Makushenko and A. I. Makhills. The instrument consisted of a rectifier, a sonic generator tuned to a frequency of 1000 cps, and an amplifier of the generated resistance for feeding the bridge, which consisted of a narrow-band amplifier and an electronic optical indicator. The instrument readings for chlorine ion content were calibrated against parallel argentometric determinations in special experiments.

The experiments were carried out in the following way. The resistance vessel was charged with a definite volume of a 2 N solution of benzenesulfonyl chloride in anhydrous acetone and cooled to 0°. Then an equivalent volume of a 2 N solution of water or alcohol (phenol) in dry acetone, which had been cooled preliminarily, was added rapidly. The vessel was hermetically sealed, its contents were mixed vigorously, and the resistance of the solution was measured.

The constancy of the instrument readings was checked periodically by parallel argentometric determinations on samples. The instrument gave a satisfactory accuracy of determination, and its sensitivity varied over a range of  $\pm 1\%$ .

The experimental data are given in Tables 3-5.

## SUMMARY

1. The reaction of benzenesulfonyl chloride with alcohols and phenols was studied.
2. A quantitative characteristic of the relative reactivity of the alcohols and phenols studied is given.

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# INVESTIGATION IN THE FURAN SERIES

## X. 2-METHYLFURAN IN SUBSTITUTIVE ADDITIONS WITH $\alpha,\beta$ -UNSATURATED ALIPHATIC KETONES

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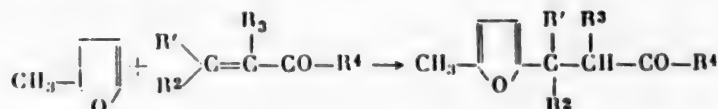
November, 1960

Original article submitted January 1, 1960

The most common methods for the synthesis of ketones of the furan series are acylation of furan by the Friedel-Crafts reaction, crotonic condensation with furfural, and organometallic synthesis with furoyl chloride [1]. However, since each of these methods has specific drawbacks, the development of new methods for synthesizing these ketones is of definite interest.

In a previous article, we reported that in the presence of sulfuric acid, 2-methylfuran reacts with mesityl oxide to form 1,1-dimethyl-1-(5-methylfuryl-2)-3-butanone [2], which refuted the previously expressed opinion that only  $\alpha,\beta$ -unsaturated ketones with an unsubstituted vinyl group can undergo substitutive addition of a furan ring [3]. Hence it followed that this reaction should be general and extend to any aliphatic  $\alpha,\beta$ -unsaturated ketone both with substituted and unsubstituted vinyl groups.

In this connection, in the present work we made a detailed study of the substitutive addition of 2-methylfuran and various  $\alpha,\beta$ -unsaturated ketones in the presence of concentrated sulfuric acid as the catalyst and established that the yields of ketones from this reaction depend little on the structure of the starting  $\alpha,\beta$ -unsaturated ketone and are 50-60% on an average. The presence of substituents at the carbon atom bound by the double bond in the  $\alpha,\beta$ -unsaturated ketone did not prevent the reaction, though the yields of the ketones were reduced somewhat. However, even with a radical like hexyl (enanthylideneacetone), the yield was 49%. The reaction proceeded quite smoothly even when there were three substituents on the two carbon atoms connected by the double bond in the  $\alpha,\beta$ -unsaturated ketone; in the reaction of 2-methylfuran and 2,3-dimethylpent-2-en-4-one, the yield of the corresponding ketone was 40%.



R <sup>1</sup>	H	H	CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	n-C <sub>4</sub> H <sub>9</sub>	iso-C <sub>4</sub> H <sub>9</sub>	n-C <sub>5</sub> H <sub>11</sub>	H	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>
R <sup>2</sup>	H	H	H	H	H	H	H	H	H	CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	CH <sub>3</sub>	
R <sub>3</sub>	H	H	H	H	H	H	H	CH <sub>3</sub>	CH <sub>3</sub>	H	H	CH <sub>3</sub>	
R <sub>4</sub>	CH <sub>3</sub>	iso-C <sub>4</sub> H <sub>9</sub>	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	CH <sub>3</sub>

The reaction procedure differed somewhat from that we described previously [5]. In the present work, the reaction was carried out without heating but with an increased amount of catalyst, which gave somewhat higher yields of ketones.

Some of the ketones we obtained had pleasant odors; in particular, 2-methyl-1-(5-methylfuryl-2)-3-butanone had an interesting but unstable flowerlike odor.

## EXPERIMENTAL

Working procedure. Into a 100-ml three-necked, round-bottomed flask with a stirrer, thermometer, and dropping funnel were placed 0.2 mole of the  $\alpha, \beta$ -unsaturated ketone and 0.2 g of hydroquinone the mixture was cooled to 5°, and concentrated sulfuric acid (from 0.05 to 2.5 ml) was added dropwise with stirring at such a rate that the temperature did not rise above 7-10°. Cooling was then stopped, and 0.2 mole of 2-methylfuran (sylvan) was added dropwise over a period of 3 hr with the temperature kept within the range of 20-25°. The mixture was stirred for a further 1.5 hr, diluted with an equal volume of ether, washed repeatedly with 2 N sodium carbonate solution and with water, and dried with calcium chloride. After removal of the ether, the ketone was vacuum distilled.

The 2,4-dinitrophenylhydrazones were prepared by boiling equimolecular amounts of 2,4-dinitrophenylhydrazine and ketone, with subsequent chromatography in benzene on alumina and recrystallization from alcohol.

1-(5-Methylfuryl-2)-3-butanone. From 14 g of methyl vinyl ketone, 16.4 g of sylvan, and 0.05 ml of sulfuric acid we obtained 15.2 g (50%) of a colorless liquid with a pleasant fruity odor.

B. p. 92.5-93° (8 mm),  $n_D^{20}$  1.4725,  $d_4^{20}$  1.0109,  $MR_D$  42.26.  $C_9H_{12}O_2F_2$ . Calculated 42.28.

Literature data: b. p. 97-98° (12 mm) [4].

5-Methyl-1-(5-methylfuryl-2)-3-hexanone. From 22.4 g of vinyl isobutyl ketone, 16.4 g of sylvan, and 0.05 ml of sulfuric acid we obtained 19.4 g (50%) of a colorless liquid.

B. p. 112-112.5° (7 mm),  $n_D^{20}$  1.4676,  $d_4^{20}$  0.9623,  $MR_D$  56.19.  $C_{12}H_{18}O_2F_2$ . Calculated 56.08.

Literature data: b. p. 134-135° (20 mm),  $n_D^{20}$  1.4640,  $d_4^{20}$  0.9569,  $MR_D$  55.83 [3].

Vinyl isobutyl ketone. Into a 1-liter, three-necked flask with a stirrer, thermometer, reflux condenser, and gas-inlet tube was placed 120.6 g of isovaleryl chloride in 200 ml of dichloroethane, 150 ml of anhydrous aluminum chloride gradually added at -5°, and a fast stream of ethylene passed into the mixture at 0° for 8 hr. The reaction product was poured onto a mixture of ice and concentrated hydrochloric acid (1:1) and the organic layer washed with 2 N hydrochloric acid and water and dried with sodium sulfate. After removal of the dichloroethane, the residue was vacuum distilled. The chloro ketone obtained was dehydrochlorinated with diethylaniline [5]. The yield was 34.7 g (31%).

B. p. 63-64° (65 mm),  $n_D^{20}$  1.4309.

Literature data: b. p. 41-42° (22 mm),  $n_D^{20}$  1.4293 [6].

1-Methyl-1-(5-methylfuryl-2)-3-butanone. From 16.8 g of ethylideneacetone [7], 16.4 g of sylvan, and 0.5 ml of sulfuric acid we obtained 19.9 g (60%) of a colorless liquid with a flowerlike odor.

B. p. 87-87.5° (7 mm),  $n_D^{20}$  1.4700,  $d_4^{20}$  0.9882.  $MR_D$  46.92.  $C_{10}H_{14}O_2F_2$ . Calculated 46.90.

Found %: C 72.25, 72.41; H 8.65, 8.52.  $C_{10}H_{14}O_2$ . Calculated %: C 72.26; H 8.49.

The 2,4-dinitrophenylhydrazone formed yellow crystals with m. p. 63-63.5°.

Found %: N 16.00, 16.28.  $C_{16}H_{18}O_5N_4$ . Calculated %: N 16.18.

1-Ethyl-1-(5-methylfuryl-2)-3-butanone. From 19.6 g of propylideneacetone [8], 16.4 g of sylvan, and 0.5 ml of sulfuric acid we obtained 18.7 g (52%) of a colorless liquid with a pleasant odor.

B. p. 72.5-73° (3 mm),  $n_D^{20}$  1.4689,  $d_4^{20}$  0.9795;  $MR_D$  51.25.  $C_{11}H_{16}O_2F_2$ . Calculated 51.52.

Found %: C 73.29, 73.53; H 8.97, 8.96.  $C_{11}H_{16}O_2$ . Calculated %: C 73.33; H 8.95.

The 2,4-dinitrophenylhydrazone formed yellow platelets with m. p. 59-60°.

Found %: N 15.62, 15.83.  $C_{17}H_{20}O_5N_4$ . Calculated %: N 15.54.

1-Propyl-1-(5-methylfuryl-2)-3-butanone. From 22.4 g of butylideneacetone [8], 16.4 g of sylvan, and 0.5 ml of sulfuric acid we obtained 17.2 g (44%) of a colorless liquid with a fruity odor.

B. p. 98-98.5° (7 mm),  $n_D^{20}$  1.4695,  $d_4^{20}$  0.9592;  $MR_D$  56.53.  $C_{12}H_{18}O_2F_2$ . Calculated 56.08.

Found %: C 74.25, 74.42; H 9.54, 9.61.  $C_{12}H_{18}O_2$ . Calculated %: C 74.19; H 9.34.

The 2,4-dinitrophenylhydrazone formed yellow needles with m. p. 75.5-76.5°.

Found %: N 15.04, 14.90.  $C_{18}H_{22}O_5N_4$ . Calculated %: N 14.96.

1-Isopropyl-1-(5-methylfuryl-2)-3-butanone. From 22.4 g of isobutylideneacetone [8], 16.4 g of sylvan, and 0.5 ml of sulfuric acid we obtained 17.6 g (45%) of a colorless liquid with a fruity odor.

B. p. 76-76.5°,  $n_D^{20}$  1.4700,  $d_4^{20}$  0.9718,  $MR_D$  55.80.  $C_{12}H_{18}O_2F_2$ . Calculated 56.08.

Found %: C 73.89, 74.14; H 9.14, 9.31.  $C_{12}H_{18}O_2$ . Calculated %: C 74.19; H 9.34.

The 2,4-dinitrophenylhydrazone formed yellow needles with m. p. 69-70°.

Found %: N 14.74, 14.89.  $C_{18}H_{22}O_5N_4$ . Calculated %: N 14.96.

1-Hexyl-1-(5-methylfuryl-2)-3-butanone. From 30.8 g of enanthylideneacetone [9], 16.4 g of sylvan, and 1 ml of sulfuric acid we obtained 23.5 g (49%) of a colorless liquid with a fruity odor.

B. p. 137-138° (7 mm),  $n_D^{20}$  1.4675,  $d_4^{20}$  0.9383;  $MR_D$  69.85.  $C_{15}H_{24}O_2F_2$ . Calculated 69.99.

Found %: C 76.30, 76.49; H 9.99, 10.10.  $C_{15}H_{24}O_2$ . Calculated %: C 76.22; H 10.23.

The 2,4-dinitrophenylhydrazone formed yellow crystals with m. p. 38-39°.

Found %: N 13.59, 13.31.  $C_{21}H_{28}O_5N_4$ . Calculated %: N 13.46.

2-Methyl-1-(5-methylfuryl-2)-3-butanone. From 16.8 g of methyl isopropenyl ketone [10], 16.4 g of sylvan, and 0.1 ml of sulfuric acid we obtained 20.9 g of a colorless liquid with a flowerlike odor.

B. p. 97-97.5° (10 mm),  $n_D^{20}$  1.4709,  $d_4^{20}$  0.9914;  $MR_D$  46.84.  $C_{10}H_{14}O_2F_2$ . Calculated 46.90.

Found %: C 72.21, 72.40; H 8.34, 8.52.  $C_{10}H_{14}O_2$ . Calculated %: C 72.26; H 8.49.

The 2,4-dinitrophenylhydrazone formed yellow crystals with m. p. 74.5-75.5°.

Found %: N 15.78, 16.00.  $C_{16}H_{18}O_5N_4$ . Calculated %: N 16.18.

1,2-Dimethyl-1-(5-methylfuryl-2)-3-butanone. From 19.6 g of 3-methylpent-2-en-4-one [11], 16.4 g of sylvan, and 0.7 ml of sulfuric acid we obtained 24.8 g (69%) of a colorless liquid with a flowerlike odor.

B. p. 106-106.5° (13 mm),  $n_D^{20}$  1.4705,  $d_4^{20}$  0.9779;  $MR_D$  51.45.  $C_{11}H_{16}O_2F_2$ . Calculated 51.52.

Found %: C 73.46, 73.60; H 9.14, 9.07.  $C_{11}H_{16}O_2$ . Calculated %: C 73.33; H 8.95.

The 2,4-dinitrophenylhydrazone formed yellow needles with m. p. 113-113.5°.

Found %: N 15.26, 15.46.  $C_{17}H_{20}O_5N_4$ . Calculated %: N 15.54.

1,1-Dimethyl-1-(5-methylfuryl-2)-3-butanone. From 19.6 g of mesityl oxide, 16.4 g of sylvan, and 2 ml of sulfuric acid we obtained 20.2 g (56%) of a colorless liquid with a camphorlike odor.

B. p. 92-92.5° (6 mm),  $n_D^{20}$  1.4705,  $d_4^{20}$  0.9725;  $MR_D$  51.71.  $C_{11}H_{16}O_2F_2$ . Calculated 51.52.

Literature data: b. p. 106-107° (15 mm),  $n_D^{20}$  1.4700,  $d_4^{20}$  0.9723 [2].

1-Methyl-1-ethyl-1-(5-methylfuryl-2)-3-pentanone. From 25.2 g of 3-methylhept-3-en-5-one [11], 16.4 g of sylvan, and 2 ml of sulfuric acid we obtained 20 g (48%) of a colorless liquid with a camphorlike odor.

B. p. 104.5-105° (6 mm),  $n_D^{20}$  1.4742,  $d_4^{20}$  0.9670;  $MR_D$  60.56.  $C_{13}H_{20}O_2F_2$ . Calculated 60.76.

Found %: C 75.15, 75.21; H 9.47, 9.55.  $C_{13}H_{20}O_2$ . Calculated %: C 74.94; H 9.68.

The 2,4-dinitrophenylhydrazone formed yellow crystals with m. p. 95-96°.

Found %: N 13.96, 13.99.  $C_{13}H_{24}O_5N_4$ . Calculated %: N 13.86.

1,1,2-Trimethyl-1-(5-methylfuryl-2)-3-butanone. From 22.4 g of 2,3-dimethylpent-2-en-4-one [12], 16.4 g of sylvan, and 2.5 ml of sulfuric acid we obtained 15.2 g (39%) of a colorless liquid with a camphorlike odor.

B. p. 108-108.5° (13 mm),  $n_D^{20}$  1.4670,  $d_4^{20}$  0.9750;  $MR_D$  56.24.  $C_{12}H_{18}O_2$ . Calculated 56.08.

Found %: C 74.27, 74.16; H 9.30, 9.32.  $C_{12}H_{18}O_2$ . Calculated %: C 74.19; H 9.34.

The 2,4-dinitrophenylhydrazone formed orange crystals with m. p. 109-110°.

Found %: N 14.87, 14.94.  $C_{13}H_{22}O_5N_4$ . Calculated %: N 14.96.

#### SUMMARY

On the example of the reaction of 2-methylfuran with various  $\alpha, \beta$ -unsaturated aliphatic ketones it was shown that substitutive addition in the furan series is a general reaction and may be used as a convenient method for the synthesis of ketones of the furan series from 1-(5-methylfuryl-2)-3-alkanones to 1,1,2-trialkyl-1-(5-methylfuryl-2)-3-alkanones which are inaccessible or difficult to prepare by other methods.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. Some or all of this periodical literature may well be available in English translation. A complete list of the cover-to-cover English translations appears at the back of this issue.

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# SYNTHESIS OF p-DIAZOACETYL DERIVATIVES OF PHENYLALANINE

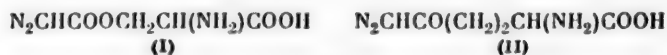
A. Ya. Berlin and K. N. Kurdyumova

Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 11, pp. 3759-3766,

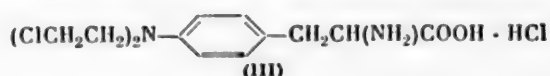
November, 1960

Original article submitted January 5, 1960

Among substances with an antitumor action there are two antibiotics of particular interest which contain diazoacetyl groups in combination with amino acid residues, namely azaserine (I) and 6-diazo-5-oxo-L-nor-leucine (II).

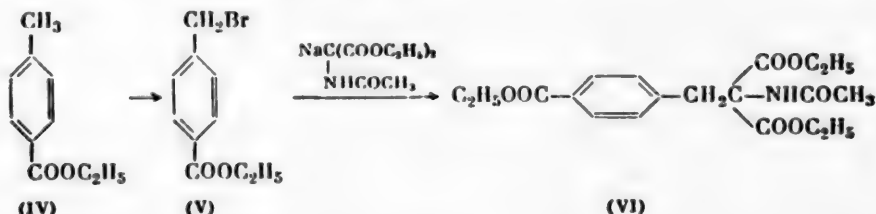


The combination of an alkylating grouping with an amino acid residue has been found effective in the case of sarcolysin (III), which is now one of the most effective chemical antitumor preparations.

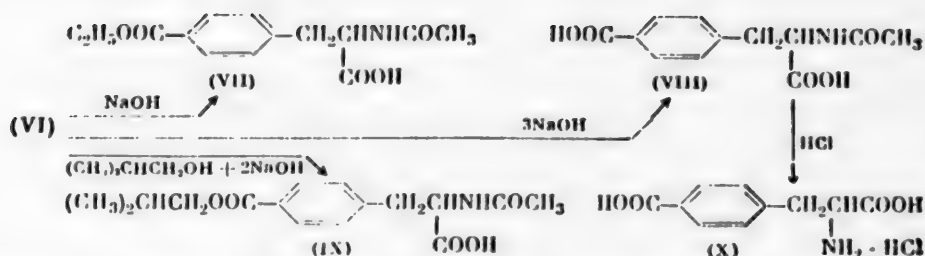


In this connection it seemed interesting to us to synthesize the analog of sarcolysin with a diazoacetyl group instead of a p-di-(β-chloroethyl)-amino group, namely, p-diazoacetylphenylalanine, or some of its simple derivatives.

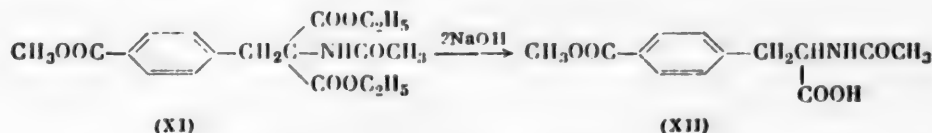
Bromination of ethyl p-toluate (IV) with bromosuccinimide in the presence of benzoyl peroxide [1] gave a good yield of ethyl p-bromomethylbenzoate (V) [2], which was condensed with sodioacetamidomalonic ester to give p-carbethoxybenzylacetamidomalonic ester (VI).



Experiments on the hydrolysis of the ester (VI), which were carried out under various conditions, showed that the rate of hydrolysis of the two aliphatic carbethoxyl groups is apparently the same and considerably exceeds the rate of hydrolysis of the carbethoxyl group in the aromatic nucleus. In actual fact, even when 1 mole of NaOH in ethanol was used, about half of the ester (VI) taken was recovered, and as the reaction product we isolated p-carbethoxy-N-acetylphenylalanine (VII), which was formed as a result of hydrolysis of both carbethoxyl groups in the acetamidomalonic ester residue and decarboxylation.

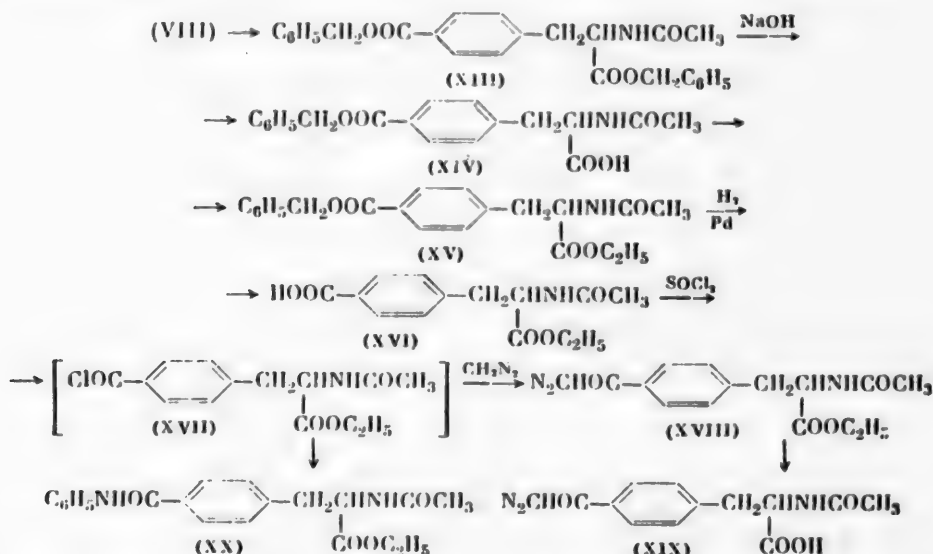


The action of three moles of NaOH yielded p-carboxy-N-acetylphenylalanine (VIII), and it was necessary to boil the latter with 20% hydrochloric acid to remove the acetyl group and form p-carboxyphenylalanine (X). In an experiment with two moles of NaOH in isobutanol, together with hydrolysis there was transesterification, and we isolated the p-isobutyl ester of p-carboxy-N-acetylphenylalanine (IX). To confirm the structure of the half ester (VII), we synthesized p-carbomethoxybenzylacetamidomalonic ester (XI) and partially hydrolyzed it. We then isolated a substance which differed from the ester (VII) and corresponded in analysis to p-carbomethoxy-N-acetylphenylalanine (XII).



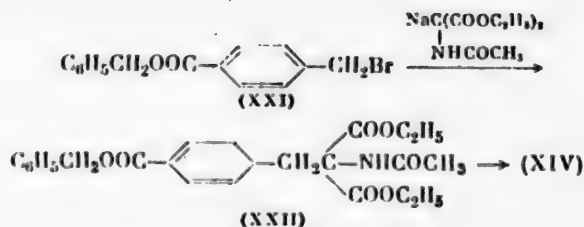
Thus, the positions of the carboxyl and carbethoxyl groups in the molecule of (VII) may be considered demonstrated by analogy.

From the dicarboxylic acid (VIII), we prepared the dibenzyl ester (XIII), which was partially hydrolyzed to give p-carbobenzoxy-N-acetylphenylalanine (XIV), analogous to the monoethyl ester (VII).



After esterification of the free carboxyl group (XIV) with alcohol [3], the ethyl benzyl ester (XV) formed was subjected to catalytic hydrogenation to yield the  $\alpha$ -ethyl ester of p-carboxy-N-acetylphenylalanine (XVI). By the action of thionyl chloride, the acid (XVI) was converted into the acid chloride (XVII), and the latter was converted into the ethyl ester of p-diazoacetyl-N-acetylphenylalanine (XVIII). Careful hydrolysis of the diazo keto ester (XVIII) formed p-diazoacetyl-N-acetylphenylalanine (XIX). For identification of the acid chloride (XVII), which was not isolated in a pure form, the anilide of the acid (XX) was prepared.

In view of the higher rate of hydrolysis of the  $\alpha$ -carbalkoxyl groups, it seemed that there was a possibility of a shorter route for the synthesis of the benzyl ester (XIV) according to the following scheme:



However, the realization of this variant was prevented by the considerable lability of the benzyl residue in the carbobenzoxy group. Thus, condensation of benzyl p-bromomethylbenzoate (XXI) with sodioacetamidomalonic ester in ethanol formed, as a result of transesterification, the triethyl ester (VI) and p-carbobenzoxybenzylacetamidomalonic ester (XXII). The latter was obtained as a result of a condensation in the absence of alcohol. Then, in the hydrolysis of the condensation product (XXII) we should have found, on the one hand, great ease of hydrolysis of the  $\alpha$ -carbalkoxyl groups and on the other hand, on the contrary, greater ease of elimination of the benzyl group [4]. It was found that the partial hydrolysis of (XXII) was actually indefinite; we obtained low yields of p-carbobenzoxy-N-acetylphenylalanine (XIV) and p-carboxy-N-acetylphenylalanine (VIII).

The formation of the benzyl ester (XIV) in the given case is definite confirmation of the accuracy of the above conclusions on the different rates of hydrolysis of the  $\alpha$ - and p-carbalkoxyl groups.

All analyses were carried out in the analytical laboratory of our institute under the direction of A. D. Chinaeva.

#### EXPERIMENTAL

p-Carboethoxybenzylacetamidomalonic ester (VI). To the sodium ethylate obtained from 3.94 g of sodium and 90 ml of anhydrous alcohol was added a solution of 37.5 g of acetamidomalonic ester in 160 ml of anhydrous alcohol. The reaction mixture was stirred for 30 min at 25–30°. Then a solution of 41.6 g of ethyl p-bromoethylbenzoate in 80 ml of dry benzene was added and the mixture stirred at 70–75° for 2 hr. After removal of the sodium bromide, from the filtrate we isolated 44.5 g (68.5%) of the ester. It had m. p. 141–141.5° (from anhydrous alcohol).

Found %: C 59.73; H 6.31.  $\text{C}_{19}\text{H}_{25}\text{O}_7\text{N}$ . Calculated %: C 60.15; H 6.64.

The colorless needles were soluble in ether and methanol and insoluble in ligroin.

p-Carboxy-N-acetylphenylalanine (VIII). To a solution of 16.6 g of p-carboethoxybenzylacetamidomalonic ester in 500 ml of alcohol was added a 10% solution of NaOH containing 5.25 g (3 equiv.) of alkali and the mixture boiled for 8 hr. After removal of the alcohol, the residue was dissolved in water and acidified to Congo with 10% hydrochloric acid. The dicarboxylic acid (VIII) precipitated as fine crystals with m. p. 238–240° (from 25% alcohol). The yield was 8 g (72.8%).

Found %: C 57.27; H 5.42.  $\text{C}_{12}\text{H}_{15}\text{O}_5\text{N}$ . Calculated %: C 57.37; H 5.21.

The colorless scaly crystals were difficultly soluble in water and moderately soluble in 25% alcohol.

Benzyl ester of p-carbobenzoxy-N-acetylphenylalanine (XIII). A solution of 8.1 g of p-carboxy-N-acetylphenylalanine (VIII) in 200 ml of benzyl alcohol was saturated with dry hydrogen chloride with cooling in ice and left at room temperature for 36 hr. After removal of the benzyl alcohol, the residue was dissolved in benzene and the solution washed with saturated bicarbonate solution and then with water. The solvent was removed and the residue recrystallized from ether. The yield was 11.3 g (81.23%) and the m. p. 91–92°.

Found %: C 72.48; H 5.57; N 3.28.  $\text{C}_{26}\text{H}_{25}\text{O}_5\text{N}$ . Calculated %: C 72.38; H 5.84; N 3.24.

The fine colorless needles were difficultly soluble in hexane, ether, and ligroin and soluble in benzene, chloroform, and alcohol.

p-Carbobenzoxy-N-acetylphenylalanine (XIV). Over a period of 30 min, 14 ml of a 10% solution of NaOH was added with stirring to a solution of 16.3 g of the benzyl ester of p-carbobenzoxy-N-acetylphenylalanine in

150 ml of benzyl alcohol on a boiling water bath and the mixture then stirred for a further 1.5 hr. After removal of the benzyl alcohol, the residue was dissolved in water and acidified to Congo with 10% hydrochloric acid, when the acid (XIV) precipitated as fine, colorless scales. The yield was 9.3 g (72.1%) and the m. p. 174-175° (from ethyl acetate).

Found %: C 66.35; H 5.54; N 4.27.  $C_{19}H_{19}O_3N$ . Calculated %: C 66.85; H 5.61; N 4.10.

The substance was soluble in alcohol and ethyl acetate.

Ethyl ester of p-carbobenzoxy-N-acetylphenylalanine (XV). To a suspension of 10 g of p-carbobenzoxy-N-acetylphenylalanine in 50 ml of anhydrous alcohol at 0° was added 2.5 ml of acetyl chloride with stirring. The mixture was stirred at 30° until the solid dissolved completely and then for a further 2 hr. After removal of the alcohol, the residue was dissolved in ethyl acetate and the solution washed with a saturated aqueous solution of bicarbonate and dried over  $Na_2SO_4$ . Removal of the ethyl acetate yielded 9.72 g (81.7%) of product with m. p. 92-93° (from ether). Recrystallization from ligroin yielded a different crystal form with m. p. 79-80°.

Found %: C 68.21; H 6.20; N 3.72.  $C_{21}H_{23}O_3N$ . Calculated %: C 68.28; H 6.27; N 3.80.

The fine white needles were difficultly soluble in benzene, hexane, ligroin, ether, and chloroform and soluble in alcohol and ethyl acetate.

Ethyl ester of p-carboxy-N-acetylphenylalanine (XVI). A solution of 8.21 g of the ethyl ester of p-carbobenzoxy-N-acetylphenylalanine (XV) in 100 ml of anhydrous alcohol was hydrogenated in the presence of 1.0 g of 5% palladium on charcoal for 2 hr. Removal of the catalyst and evaporation of the solvent yielded 5.05 g (80.5%) of product. The lustrous scales had m. p. 187-188° (from ethyl acetate).

Found %: C 60.11; H 6.06; N 5.37.  $C_{14}H_{17}O_3N$ . Calculated %: C 60.20; H 6.13; N 5.02.

The substance was soluble in acetone and alcohol and difficultly soluble in ether and chloroform.

Acid chloride of the ethyl ester of p-carboxy-N-acetylphenylalanine (XVII). With cooling in ice and stirring 2.0 ml (25% excess) of thionyl chloride was added to 5.05 g of the ethyl ester of p-carboxy-N-acetylphenylalanine (XVI) in 50 ml of dry chloroform. The mixture was then heated at 50-52° on a water bath for 15 min, when the acid (XVI) dissolved completely and the solution became slightly yellow. The solvent and excess thionyl chloride were removed in vacuum at 40° and the residue treated with dry benzene with subsequent distillation. The solid acid chloride obtained was used without purification.

Anilide of the ethyl ester of p-carboxy-N-acetylphenylalanine (XX). A solution of 0.24 g (threefold excess) of aniline in 5 ml of dry chloroform was added with cooling to a solution of 0.24 g of the acid chloride (XVII) in 5 ml of dry chloroform. The precipitate was collected and washed on the filter with 1% hydrochloric acid and water. We obtained 0.21 g of product with m. p. 190-191° (from alcohol and ethyl acetate).

Found %: C 67.40; H 6.10; N 8.03.  $C_{20}H_{22}O_4N_2$ . Calculated %: C 67.78; H 6.26; N 7.90.

The fine, colorless needles were soluble in methanol and difficultly soluble in ether.

Ethyl ester of p-diazoacetyl-N-acetylphenylalanine (XVIII). The acid chloride (XVII) obtained from 5.05 g of the ethyl ester of p-carboxy-N-acetylphenylalanine was dissolved in 50 ml of dry chloroform and this solution added dropwise at 0° with stirring to an ether solution of a fivefold excess of diazomethane. When approximately half of the solution of the acid chloride (XVII) had been added, a yellow crystalline substance began to precipitate from the reaction mixture. When all the acid chloride (XVII) had been added, the reaction mixture was stirred for a further 2 hr without cooling. The precipitate was then collected and the solvent removed completely in vacuum without heating. We obtained 4.5 g (83.0%) of product with m. p. 134-135° (decomp., from 50% alcohol).

Found %: C 59.41; H 5.75; N 13.82.  $C_{15}H_{17}O_4N_3$ . Calculated %: C 59.40; H 5.65; N 13.88.

The light yellow crystals were soluble in alcohol and difficultly soluble in ether.

p-Diazoacetyl-N-acetylphenylalanine (XIX). To a solution of 1.0 g of the ethyl ester of p-diazoacetylphenylalanine in alcohol was added a 10% solution of NaOH (1 equiv.) at 0° and the mixture left at 0° for 48 hr. The color of the solution then became dark red. The reaction mixture was then adjusted to pH 6.5 with dilute

hydrochloric acid and the solvent removed in vacuum without heating. The residue was dissolved in anhydrous alcohol and absolute ether added to the solution. The flocculent precipitate was collected and the filtrate evaporated to dryness without heating. We obtained a finely crystalline yellow powder, which was recrystallized from a mixture of anhydrous methanol and ether and then from 75% alcohol. The yield was 0.1 g and the m. p. 103-106° (decomp.). The substance contained 1 mole of water of crystallization.

Found %: C 52.59; H 5.29; N 14.40.  $C_{13}H_{13}O_4N_3 \cdot H_2O$ . Calculated %: C 53.23; H 5.15; N 14.30.

The yellow needles were soluble in methanol and alcohol and insoluble in ether.

p-Carbomethoxybenzylacetamidomalonic ester (XI). A solution of 20.6 g of methyl p-bromomethylbenzoate in 40 ml of anhydrous alcohol was added to sodioacetamidomalonic ester (from 2.06 g of sodium and 19.45 g of acetamidomalonic ester in 70 ml of anhydrous alcohol). The reaction mixture was stirred at 70-75° for 2 hr. The precipitate was removed by filtration and the filtrate cooled to yield 15.6 g (50.4%) of product with m. p. 121-122° (from methanol).

Found %: C 58.95; H 5.95; N 3.99.  $C_{18}H_{23}O_7N$ . Calculated %: C 59.17; H 6.34; N 3.83.

The needlelike crystals were soluble in alcohol, methanol, acetone, ether, and benzene.

p-Carbomethoxy-N-acetylphenylalanine (XII). Over a period of 2 hr, a 10% solution of NaOH (2 equiv.) was added with stirring to a solution of 2.0 g of p-carbomethoxybenzylacetamidomalonic ester in 30 ml of methanol at 50-55°. After removal of the solvent, the residue was dissolved in water, the solution filtered, and the filtrate acidified to Congo with 10% hydrochloric acid to form a precipitate. The yield was 0.9 g. Recrystallization from ethyl acetate gave 0.3 g of the dicarboxylic acid (VIII) (m. p. 238-240°) and 0.25 g of p-carbomethoxy-N-acetylphenylalanine (XII) with m. p. 171-172° (from acetone).

Found %: C 58.82; H 5.74.  $C_{13}H_{15}O_5N$ . Calculated %: C 58.86; H 5.70.

The colorless needles were soluble in alcohol, methanol, ethyl acetate, and acetone and difficultly soluble in ether.

p-Carbomethoxy-N-acetylphenylalanine (VII). An alcohol solution of NaOH (1 equiv.) was added to a solution of 2.0 g of p-carbomethoxybenzylacetamidomalonic ester (VI) in 25 ml of ethanol. The mixture was boiled for 3.5 hr. The reaction mixture was then diluted with twice its volume of water and extracted with ether. From the ether solution we isolated 0.83 g of the starting material (VI). Acidification of the aqueous solution with 10% hydrochloric acid yielded an oil, which solidified when treated with absolute ether. The yield was 0.5 g and the m. p. 151-152° (from methanol and acetone).

Found %: C 59.82; H 5.98; N 5.30.  $C_{14}H_{17}O_5N$ . Calculated %: C 60.21; H 6.13; N 5.01.

The substance was soluble in methanol, alcohol, and dioxane; difficultly soluble in ethyl acetate and acetone; and insoluble in ether, ligroin, chloroform, and benzene.

Isobutyl ester of p-carboxy-N-acetylphenylalanine (IX). A mixture of 2.0 g of p-carbomethoxybenzylacetamidomalonic ester (VI), 30 ml of isobutanol, and an alcohol solution of NaOH (2 equiv.) was heated at 100-105° for 3.5 hr. The mixture was diluted with three times its volume of water and acidified to Congo with 10% hydrochloric acid. This liberated 1.9 g of oil, which crystallized when triturated with absolute ether. The yield was 0.19 g and the m. p. 167-167.5° (from ethyl acetate, acetone, and 30% alcohol).

Found %: C 62.14; H 6.63; N 4.58.  $C_{16}H_{21}O_5N$ . Calculated %: C 62.53; H 6.89; N 4.55.

The fine needles were soluble in alcohol, methanol, ethyl acetate, and acetone and difficultly soluble in ether.

p-Carboxyphenylalanine hydrochloride (X). When 0.22 g of p-carboxyacetamidophenylalanine (VIII) was boiled with 15 ml of 20% hydrochloric acid for 3 hr, the solid (VIII) first dissolved, and then the hydrochloride precipitated. The yield was 0.15 g and the m. p. 287-292° (decomp., from 10% hydrochloric acid).

Found %: C 48.87; H 5.06; N 5.72; Cl 14.68.  $C_{10}H_{12}O_4NCl$ . Calculated %: C 48.89; H 4.92; N 5.70; Cl 14.44.

The colorless crystals were insoluble in water, alcohol, and acetic acid and soluble in dilute alkali.



p-Carbobenzoxymethylacetamidomalonic ester (XXII). To an alcohol solution of Na-acetamidomalonic ester (from 0.31 g of sodium and 2.9 g of acetamidomalonic ester in 25 ml of anhydrous alcohol) was added dry benzene and the excess alcohol and benzene removed completely in vacuum. To the residue was added 20 ml of dry benzene and then a solution of 5.0 g of benzyl p-bromomethylbenzoate in 20 ml of dry benzene. The mixture was then stirred for 6 hr at 80° (bath temperature). After removal of the benzene, the residue was treated with water and the insoluble substance collected. The yield was 3.48 g (47.5%) and the m. p. 160-161° (from acetone and methanol).

Found %: C 64.97; H 6.12; N 3.18.  $C_{24}H_{27}O_7N$ . Calculated %: C 65.29; H 6.16; N 3.17.

The colorless crystals were soluble in alcohol, methanol, acetone, and ethyl acetate.

When this synthesis was attempted in alcohol there was transesterification and the formation of the already known p-carbomethoxybenzylacetamidomalonic ester (VI) with m. p. 137-138.5° (from anhydrous alcohol). A mixed melting point with an authentic sample was not depressed.

Found %: C 60.24; H 6.66; N 3.74.  $C_{19}H_{25}O_7N$ . Calculated %: C 60.15; H 6.64; N 3.69.

Hydrolysis of p-carbobenzoxymethylacetamidomalonic ester. A 1.0-g sample of p-carbobenzoxymethylacetamidomalonic ester (XXII) was hydrolyzed by stirring with 5 ml of benzyl alcohol and a 10% aqueous solution of NaOH (2 equiv.) on a boiling water bath for 2 hr. After being heated, the reaction mixture was poured into water and extracted with benzene. The aqueous solution was acidified to Congo with 10% hydrochloric acid to form a precipitate. The yield was 0.42 g. Recrystallization from ethyl acetate gave 1.0 g of the dicarboxylic acid (VIII) and 0.14 g of a substance with m. p. 172-173° (from ethyl acetate), which did not depress the melting point of p-carbobenzoxymethyl-N-acetylphenylalanine (XIV).

#### SUMMARY

1. The ethyl ester of p-diazoacetyl-N-acetylphenylalanine was synthesized from ethyl p-bromomethylbenzoate through p-carbomethoxybenzylacetamidomalonic ester, p-carboxy-N-acetylphenylalanine, the benzyl ester of p-carbobenzoxymethyl-N-acetylphenylalanine, p-carbobenzoxymethyl-N-acetylphenylalanine, the ethyl ester of p-carbobenzoxymethyl-N-acetylphenylalanine, the  $\alpha$ -ethyl ester of p-carboxy-N-acetylphenylalanine, and the acid chloride of the  $\alpha$ -ethyl ester of p-carboxy-N-acetylphenylalanine.

2. Hydrolysis of the ether ester of p-diazoacetyl-N-acetylphenylalanine yielded p-diazoacetyl-N-acetylphenylalanine (the diazoacetyl analog of N-acetylsarcosine).

3. The hydrolysis of the methyl, ethyl, and benzyl esters of p-carboxybenzylacetamidomalonic ester was studied.

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# INVESTIGATIONS IN THE ANTHRAQUINONE SERIES

## XXXI. SULFONIC ACIDS OF TRANS-DIBENZPYRENEQUINONE\*

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 11, pp. 3766-3772,

November, 1950

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Up to now the sulfonation of trans-dibenzpyrenequinone has not been studied systematically. Some data on the preparation of sulfonic acids of dibenzpyrenequinone as intermediates for hydroxy compounds may be

found in patents [1]. A. M. Lukin, in establishing that sulfonoxides  $\left[ \begin{array}{c} R' \\ \diagup \\ R \end{array} \right] \text{CO-SO}_3$  were formed as inter-

mediate products in the reaction of polycyclic ketones  $\left[ \begin{array}{c} R' \\ \diagup \\ R \end{array} \right] \text{CO}$  with a sulfonating agent [2], isolated a

monosulfonic acid of trans-dibenzpyrenequinone as the zinc salt.

An important factor in the sulfonation of dibenzpyrenequinone is the temperature. Neither sulfuric acid monohydrate nor 20% oleum sulfonates dibenzpyrenequinone at 100°. Sulfonation with a large excess of the monohydrate is possible at 175-180° over a period of 12 hr with the formation of a mixture of mono- and disulfonic acids of dibenzpyrenequinone. Sulfonation with oleum also proceeds with difficulty, and complete reaction is possible at 150-160° in a period of 1 hr with a 50% excess of oleum, calculated on the introduction of two sulfonic acid groups. Reducing the excess of oleum to 10% left up to 10% of unchanged starting material (table). Lowering the temperature to 140° with a large excess of oleum and an increase in the time to 5 hr reduced the yield of disulfonic acid to 50%. Sulfonation with the theoretical amount of 20% oleum or a 50% excess, calculated on the introduction of one sulfonic acid group, at 150° and for various times led to the formation of both disulfonic acid and monosulfonic acid with part of the dibenzpyrenequinone remaining unchanged. It was difficult to stop the sulfonation at the monosulfonic acid, and despite unchanged dibenzpyrenequinone, the reaction readily formed the disulfonic acid. This behavior of dibenzpyrenequinone is reminiscent to some extent of the sulfonation of anthraquinone [3]. As the data in the table show, sulfonation with oleum, especially to the monosulfonic acid, was accelerated somewhat by mercury salts. Sulfonation in the presence of sodium sulfate produced somewhat more complete disulfonation.

By isolating the disulfonic acid of dibenzpyrenequinone as the disodium salt and also by preparing some of its other salts with metals and aromatic amines, we established that the corresponding derivatives of the disulfonic acid obtained by sulfonation with mercury and also without it were identical. Despite the fact that the colors of the dry disodium salts of the disulfonic acids of dibenzpyrenequinone differed somewhat (yellow-brown from sulfonation with mercury and yellow-orange without mercury), their visible and ultraviolet absorption spectra were identical: The disodium salt in water\*\* had  $\lambda_{\text{max}}$  450 and 476 m $\mu$ , and the disodium salt in H<sub>2</sub>SO<sub>4</sub>

\*See Zhur, Obshchei Khim, 30, 3464 (1960) for communication XXX.

\*\* The spectra were plotted by Yu. A. Kolesnik.

Sulfonation of Dibenzpyrenequinone\* [8.3 g (0.025 mole) of dibenzpyrenequinone and 20% oleum]

Expt. No.	SO <sub>3</sub> (mole)	Temp.	Time (hr)	Products (%)		
				unchanged dibenzpyrenequinone	monosulfonic acid	disulfonic acid
1	0.04	150°	1	41.0	15.0	43.3
2	0.04	150	5	12.0	34.0	45.6
3**	0.04	150	1	10.0	42.1	45.3
4	0.052	150	1	8.5	—	91.0
5**	0.052	150	1	8.5	—	91.5
6***	0.052	150	1	4.0	—	96.0
7	0.079	150	1	—	—	97.0
8**	0.079	150	1	—	—	100.0
9	0.079	150	5	50.0	—	50.0
10	0.025	160	5	45.7	6.4	29.1
11****	0.075	160	4	—	—	92.8
12	30.0 (mono-hydrate)	175	10	—	15.0	83.0

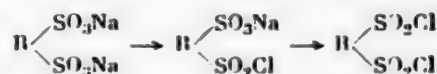
\* Parallel experiments gave variations in yield of up to 5%.

\*\* With 10% HgSO<sub>4</sub>.

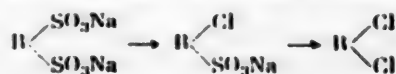
\*\*\* With 10% Na<sub>2</sub>SO<sub>4</sub>.

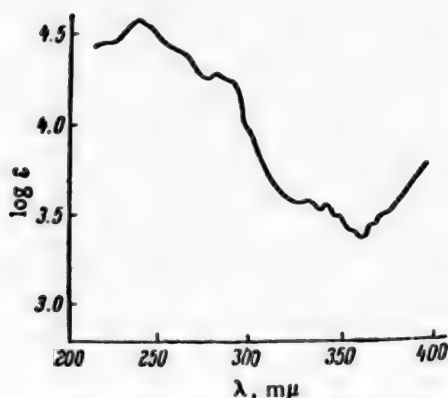
\*\*\*\* With 40% oleum.

(d 1.84) had  $\lambda_{\max}$  530 m $\mu$ . The nature of the ultraviolet absorption spectrum of the disodium salt is shown in the figure. Thus, in contrast to the sulfonation of anthraquinone, the positions of the sulfonyl groups introduced into dibenzpyrenequinone are not changed by mercury salts. The conversions of the disulfonic acid of dibenzpyrenequinone described below were carried out with the disodium salt obtained by sulfonation both with mercury and without it, and were also found to be identical. A comparison of the absorption spectra in sulfuric acid of trans-dibenzpyrenequinone (violet color) and the disodium salt of the disulfonic acid obtained (red color) shows the hypsochromic effect of the sulfonic acid groups, which displace the absorption maximum by 38 m $\mu$  (from 568 to 530 m $\mu$ ). The disodium salt of dibenzpyrenequinonedisulfonic acid was readily soluble in water and dyed wool and caprone fiber a bright golden yellow from an acid solution. The fastness of the dye was high to light, but low to soap and water. Heating the disodium salt of dibenzpyrenequinonedisulfonic acid with sulfuric acid of various concentrations to 180° for 3 hr both with mercury and without it did not lead to hydrolysis of the sulfonic acid groups, while traces of dibenzpyrenequinone were formed in 70–80% sulfuric acid at 225°. Heating the substance at 225° for 3 hr in 1% sulfuric acid in sealed tubes both with mercury and without it did not lead to hydrolysis of dibenzpyrenequinonedisulfonic acid either. Heating a mixture of the dry disodium salt of dibenzpyrenequinonedisulfonic acid with a twofold excess of PCl<sub>5</sub> at 225° led to a mixture of reaction products in low yields according to the following scheme, where R is a dibenzpyrenequinone residue:



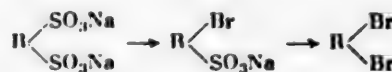
The acid chlorides dissolved only in sulfuric acid and they could not be separated. As dibenzpyrenequinonedisulfonic acid was quite resistant to the action of strong oxidative chlorinating agents, we treated it with chlorate in a hydrochloric–sulfuric acid mixture as is used for the replacement of sulfonic acid groups by chlorine in anthraquinonesulfonic acids [4]. In our case the reaction proceeded with great difficulty, and heating at 102° for 2 hr led to 16% of monochlorodibenzpyrenequinonesulfonic acid and 8% of dichlorodibenzpyrenequinone (violet color in sulfur acid) with unchanged starting material remaining in solution.





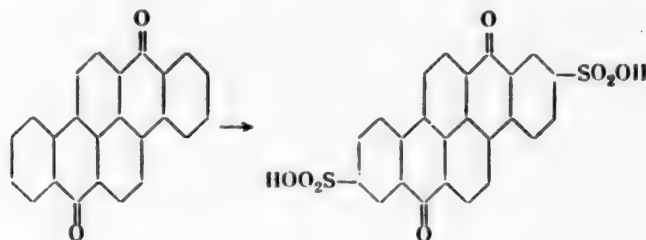
Absorption spectrum of the disodium salt of dibenzpyrenequinone- $\beta,\beta'$ -disulfonic acid in water ( $\log \epsilon$  4.58,  $\lambda_{\max}$  236 m $\mu$ ;  $\log \epsilon$  4.42,  $\lambda_{\max}$  262 m $\mu$ ).

The reaction of dibenzpyrenequinonedisulfonic acid with potassium bromate in sulfuric acid and potassium bromide proceeded analogously. While the bulk of the material remained unchanged, up to 10-12% of bromo sulfonic acid and 5-6% of dibromodibenzpyrenequinone were obtained.



A comparison of the absorption spectra in sulfuric acid of transdibenzpyrenequinone and the dibromodibenzpyrenequinone obtained showed a bathochromic displacement of the absorption maximum of 22 m $\mu$  (from 568 to 590 m $\mu$ ) due to the bromine atoms introduced. The absorption spectrum of the dibromodibenzpyrenequinone obtained from the disulfonic acid was identical with that of the purified dye, vat golden yellow KKh, which is brominated dibenzpyrenequinone [5] ( $\lambda_{\max}$  590 m $\mu$  (in  $\text{H}_2\text{SO}_4$ )). Thus, the positions of the sulfonic acid groups in dibenzpyrenequinonedisulfonic acid correspond to the positions of

the bromine atoms in vat golden yellow KKh. Since it is considered that in the bromination of dibenzpyrenequinone, the bromine atoms enter the  $\beta,\beta'$ -positions, which are most reactive [6], the structure of the disulfonic acid obtained corresponds to dibenzpyrenequinone- $\beta,\beta'$ -disulfonic acid.



The effect of the sulfonic acid groups on the color of dibenzpyrenequinone is opposite to and stronger than that of the bromine atoms. Open alkaline fusion at 220-300° with potassium hydroxide of both the disodium salt of dibenzpyrenequinonedisulfonic acid and dibromodibenzpyrenequinone (vat golden yellow KKh) yielded identical hydroxy derivatives (brown color in sulfuric acid,  $\lambda_{\max}$  466 m $\mu$  in alcohol).

## EXPERIMENTAL

1. 3,4,8,9-Dibenzpyrene-5,10-quinone was obtained by purification of the technical product (vat golden yellow KKh) by repeated precipitation from sulfuric acid and extraction of the washed and dried product with boiling dioxane. It dissolved in concentrated sulfuric acid with a violet color ( $\lambda_{\max}$  568 m $\mu$ ) and melted at 365°.

2. Sulfonation of dibenzpyrenequinone. Into a 100-ml three-necked flask with a stirrer, reflux condenser, and mercury seal on an oil bath was placed sulfuric acid, and dry dibenzpyrenequinone (0.025 mole) gradually added at 50-60°. The mass was heated to a given temperature and kept there for a determined time until a sample was soluble in dilute sodium hydroxide. After the sulfonation, the mixture was cooled to 50°, poured onto ice, and then heated to 70-80°. The insoluble portion was collected by filtration and washed with warm water and then boiling 1% sodium hydroxide solution. The residue on the filter was unreacted dibenzpyrenequinone. The alkaline solution was made weakly acid with hydrochloric acid and then treated with saturated zinc chloride solution to liberate the zinc salt, or with sodium sulfate to form the sodium salt of dibenzpyrenequinonemonosulfonic acid. The main acid mother solution was boiled with activated charcoal, the sulfuric acid removed as calcium sulfate, and the sulfonic acids isolated as the sodium salt by evaporation of the solution. The zinc salt of dibenzpyrenequinonemonosulfonic acid crystallized from water as fine, yellow-orange crystals.

Found %:  $\text{H}_2\text{O}$  9.2.  $\text{C}_{48}\text{H}_{22}\text{O}_{10}\text{S}_2\text{Zn} \cdot 5\text{H}_2\text{O}$ . Calculated %:  $\text{H}_2\text{O}$  9.7.

Found %: Zn 7.8.  $\text{C}_{48}\text{H}_{22}\text{O}_{10}\text{S}_2\text{Zn}$ . Calculated %: Zn 7.48.

The sodium salt crystallized from water as yellow-orange rods with various amounts of water of crystallization.

Found %:  $\text{H}_2\text{O}$  3.5.  $\text{C}_{24}\text{H}_{11}\text{SNa} \cdot \text{H}_2\text{O}$ . Calculated %:  $\text{H}_2\text{O}$  3.5.

Found %:  $\text{H}_2\text{O}$  10.3.  $\text{C}_{24}\text{H}_{11}\text{O}_5\text{SNa} \cdot 3\text{H}_2\text{O}$ . Calculated %:  $\text{H}_2\text{O}$  11.0.

Found %: C 54.12; H 2.24; Na 4.9.  $\text{C}_{24}\text{H}_{11}\text{O}_5\text{SNa}$ . Calculated %: C 53.73; H 2.0; Na 5.3.

The sodium salt of dibenzpyrenequinonedisulfonic acid was reprecipitated repeatedly from aqueous solution with alcohol and then recrystallized from water. Preliminary experiments in which a 0.1 N solution of the disodium salt of dibenzpyrenequinonedisulfonic acid (A) was mixed with 0.1 N solutions of inorganic salts with various cations showed that the barium, lead, and aluminum salts were most difficultly soluble. The potassium, calcium, magnesium, zinc, cobalt, nickel, copper, iron (ferrous and ferric), and mercurous salts were readily soluble.

Sodium salt. The substance crystallized from water as fine yellow or brownish yellow needles with various water contents. It was insoluble in alcohol, acetic acid, acetone, and dichloroethane. Its solubility was 0.7 g in 100 ml of water (18°).

Found %:  $\text{H}_2\text{O}$  11.2.  $\text{C}_{24}\text{H}_{10}\text{O}_8\text{S}_2\text{Na}_2 \cdot 4\text{H}_2\text{O}$ . Calculated %:  $\text{H}_2\text{O}$  11.84.

Found %:  $\text{H}_2\text{O}$  6.2.  $\text{C}_{24}\text{H}_{10}\text{O}_8\text{S}_2\text{Na}_2 \cdot 2\text{H}_2\text{O}$ . Calculated %:  $\text{H}_2\text{O}$  6.29.

Found %: C 53.61; H 2.13; Na 8.78.  $\text{C}_{24}\text{H}_{10}\text{O}_8\text{S}_2\text{Na}_2$ . Calculated %: C 53.73; H 1.86; Na 8.58.

The barium salt was obtained in the reaction of a solution of (A) with barium chloride. It was difficultly soluble in water and alcohol and crystallized as fine, yellowish brown crystals.

Found %:  $\text{H}_2\text{O}$  3.91.  $\text{C}_{24}\text{H}_{10}\text{O}_8\text{S}_2\text{Ba} \cdot 1.5\text{H}_2\text{O}$ . Calculated %:  $\text{H}_2\text{O}$  4.12.

Found %: Ba 22.0.  $\text{C}_{24}\text{H}_{10}\text{O}_8\text{S}_2\text{Ba}$ . Calculated %: Ba 21.88.

The aluminum salt was obtained by the reaction of a solution of (A) with aluminum sulfate. It was difficultly soluble in water and crystallized from this solvent as fine, yellowish brown grains.

Found %:  $\text{H}_2\text{O}$  15.52.  $\text{C}_{24}\text{H}_{30}\text{O}_{24}\text{S}_6\text{Al}_2 \cdot 15\text{H}_2\text{O}$ . Calculated %:  $\text{H}_2\text{O}$  15.05.

Found %: Al 3.78.  $\text{C}_{24}\text{H}_{30}\text{O}_{24}\text{S}_6\text{Al}_2$ . Calculated %: Al 3.54.

All the salts of dibenzpyrenequinonedisulfonic acid obtained by sulfonation of dibenzpyrenequinone with mercury and without it were identical. All the salts dissolved in concentrated sulfuric acid with a red color.

Salts with amines. In a number of cases, treatment of a 0.2 N solution of (A) with an equimolecular amount of an aromatic amine hydrochloride yielded a precipitate of the salt of the amine and dibenzpyrenequinonedisulfonic acid. The salt with aniline was readily soluble in water. The salts with o-nitroaniline (light yellow needles), m-nitroaniline (microscopic light yellow needles), p-toluidine (reddish yellow needles), benzylthiuronium long gray-yellow needles, and o-toluidine (reddish yellow needles) were soluble in hot water, while the salts with  $\alpha$ -naphthylamine (lemon yellow needles),  $\beta$ -naphthylamine (yellow needles), and benzidine (golden yellow rods or tablets) were very difficultly soluble in hot water.

#### p-Toluidine salt.

Found %:  $\text{H}_2\text{O}$  10.76.  $\text{C}_{24}\text{H}_{12}\text{O}_8\text{S}_2 \cdot \text{C}_7\text{H}_7\text{NH}_2 \cdot 5\text{H}_2\text{O}$ . Calculated %:  $\text{H}_2\text{O}$  11.3.

Found: nitrite number 262 (ml of 1 N  $\text{NaNO}_2$  per 100 g of substance).  $\text{C}_{24}\text{H}_{12}\text{O}_8\text{S}_2(\text{C}_7\text{H}_7\text{NH}_2)_2$ . Calculated nitrite number 283.

### 3. Replacement of sulfonic acid groups by chlorine and bromine in dibenzpyrenequinonedisulfonic acid.

a) A 2-g sample of the disodium salt of dibenzpyrenequinonedisulfonic acid in a mixture of hydrochloric and sulfuric acids (64 mequiv. of HCl and 560 mequiv. of  $\text{H}_2\text{SO}_4$ ) was treated with 15 ml of 20% potassium chlorate solution for 2 hr at 102°. The reddish yellow precipitate was collected from the hot solution and washed with

alcohol on the filter until neutral to Congo paper. The product was dried in a desiccator over alkali and the yield was 30% of the weight of the salt used for chlorination. The product was extracted with dioxane. The insoluble residue crystallized from pyridine or nitrobenzene as needles. The substance did not sublime or melt and dissolved in concentrated sulfuric acid with a violet color; the color of a solution in sodium hydroxide reduced with hydrosulfite (vat) was cherry red.

Found %: Cl 7.25; Na 4.90.  $C_{24}H_{10}O_2ClSO_3Na_2$ . Calculated %: Cl 7.57; Na 4.88.

From the dioxane solution and also the alcohol used for washing the crude reaction product we isolated a small amount of a greasy product, which was difficultly soluble in various solvents and most soluble in pyridine, nitrobenzene, toluene, and dioxane. It sublimed slightly as dark yellow needles, which dissolved in concentrated sulfuric acid with a violet color.

Found %: Cl 22.1.  $C_{24}H_{10}O_2Cl_2$ . Calculated %: Cl 23.58.

The acid mother solution from chlorination contained unreacted dibenzpyrenequinonedisulfonic acid. Changing the chlorination conditions did not lead to an unequivocal reaction or an appreciable increase in the yields.

b) A 1-g sample of the disodium salt of dibenzpyrenequinonedisulfonic acid in a solution of 1 g of potassium bromide in 100 ml of 2 N sulfuric acid was treated with 20 ml of 10% potassium bromate solution, which was gradually introduced under the liquid, at 102° for 1.5-2 hr. The yellow-red precipitate was collected from the hot solution and washed with hot water and alcohol until neutral to Congo paper. Unchanged salt was isolated from the aqueous alcohol solution and also from the acid mother solution. The product that was insoluble in hot water and alcohol was extracted with dioxane.

The residue dissolved in concentrated sulfuric acid with a violet color. The vat was cherry red.

Found %: Br 15.02; Na 5.23.  $C_{24}H_{10}O_2BrSO_3Na$ . Calculated %: Br 15.57; Na 4.46.

Distillation of the solvent from the dioxane solution yielded a greasy product, which solidified when dried in a desiccator over alkali, and dissolved in concentrated sulfuric acid with a blue color. The vat was red.

Found %: C 59.32; H 2.28; Br 31.72.  $C_{24}H_{10}O_2Br_2$ . Calculated %: C 58.79; H 2.04; Br 32.62.

Changing the bromination conditions did not lead to an unequivocal reaction or an appreciable increase in the yields.

4. Alkali fusion of the disulfonic acid and dibromodibenzpyrenequinone. A 2-g sample of the disodium salt of dibenzpyrenequinonedisulfonic acid was fused with 12 g of KOH and 1.2 ml of water at 300° for 1 hr. The alkaline melt was dissolved in water and the solution filtered free from the dibenzpyrenequinone formed (up to 28%) and acidified to liberate the dihydroxydibenzpyrenequinone (up to 18.5-19.5%). From the acid solution we isolated unchanged disodium salt of dibenzpyrenequinonedisulfonic acid (up to 50%). An analogous fusion of dibromodibenzpyrenequinone (vat golden yellow KKh) at 220° for 1 hr led to 40% of dihydroxydibenzpyrenequinone and considerable tar formation. The alkaline fusion of neither of the substances was investigated in detail.

#### SUMMARY

The sulfonation of trans-dibenzpyrenequinone was studied and the disulfonic acid prepared. Some conversions of this disulfonic acid, to which the structure of dibenzpyrenequinone- $\beta,\beta'$ -disulfonic acid was assigned, were carried out.

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## INTRAMOLECULAR HYDROGEN BOND AND ULTRAVIOLET ABSORPTION SPECTRA

### VIII. ELECTRONIC SPECTRA OF N-METHYL AND N-PHENYL DERIVATIVES OF NITROBENZENE

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Khar'kov Polytechnic Institute

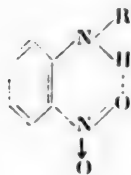
Translated from *Zhurnal Obshchei Khimii*, Vol. 30, No. 11, pp. 3773-3782,

November, 1960

Original article submitted July 7, 1959

Judging by data on dipole moments [1], in ortho isomers of disubstituted benzenes with the composition  $\text{NO}_2\text{C}_6\text{H}_4\text{NHR}$ , where  $\text{R} = \text{CH}_3$  and  $\text{C}_6\text{H}_5$ , there is quite a strong intramolecular hydrogen bond involving the hydrogen of the NH group.

In order to check the applicability of the previously established [2] features of the manifestation of this type of bond in the electronic spectra of molecules, we measured the absorption in the region of 2200-6000 Å of N-methyl-, N,N-dimethyl-, N-phenyl-, and N-methyl-N-phenylanilines and their ortho-, meta-, and para-nitro derivatives in various solvents: hexane (h), dioxane (d), ethanol (e), acetone (ac), 2N ethanol solution of sodium alcoholate (et), 98% sulfuric acid (csa), 9.8% aqueous solution of sulfuric acid (dsa), and HCl-saturated ethanol (HCl). The absorption curves of some of these nitro derivatives were measured previously [3], but only in ethanol. The measurements were made with an SF-4 spectrophotometer. The characteristics of the absorption curves obtained (the wavelengths  $\lambda$  in m $\mu$  and  $\log \epsilon$  of the maxima and inflections of the bands) for derivatives of N-methylaniline are given in Table 1 and for derivatives of diphenylamine in Table 2. The tables also give oscillation strengths  $f$  and the width  $b$  at ( $\epsilon_{\text{max}}/2$ ) or at  $\log \epsilon = 3.0$  for some bands. The absorption curves in hexane are given in Figs. 1-4, and those in the other solvents were given in [4]. The data obtained for the position of the band maxima in ethanol agree satisfactorily, as a rule, with the measurements of other authors [3].



The monosubstituted derivatives of benzene studied showed two intense absorption bands in hexane between 286-296 m $\mu$  and 230-254 m $\mu$ , which differed appreciably in width. Two bands of this type are observed for almost all monosubstituted benzenes [5], and the longwave band is connected with the electronic transitions  $A_{1g} \rightarrow B_{2u}$  localized in the benzene ring [6]. This band, whose center for benzene is at 254 m $\mu$  ( $\epsilon$  200), is gradually displaced toward longer wavelengths with an increase in the electron-donor properties of the substituent and is evidently at the longest wavelengths for the methylamino, dimethylamino, phenylamino, and methylphenylamino derivatives of benzene examined. Precisely this explanation of the nature of this band is supported by the following: the considerable increase in the intensity of its maximum with an increase in the number of benzene rings (diphenylamine and N-methyldiphenylamine in comparison with methyl- and dimethylanilines, respectively); the comparatively slight effect of polar solvents on the position of this band (a displacement of not more than 2 m $\mu$  as a rule); the sharp fall in intensity and the displacement toward short wavelengths to values of  $\lambda$  and  $\epsilon$  close to those for this band for unsubstituted benzene during salt formation involving the p-electrons of the amino group nitrogen, whereby in dilute acids (9.8% sulfuric acid or HCl-saturated ethanol), apparently due to incomplete salt formation, the curves of some monosubstituted derivatives show bands of  $A_{1g} \rightarrow B_{2u}$  transitions.

TABLE 1

Characteristics of the Bands and Inflections of the Absorption Curves of Disubstituted Derivatives with the Composition  $XC_6H_4N(Y)CH_3$ 

Compound		Solvent	Longwave Inflection		A			A <sub>1g</sub> → B <sub>1u</sub>				B <sub>C<sub>6</sub>H<sub>4</sub>NO<sub>2</sub></sub>			B <sub>C<sub>6</sub>H<sub>4</sub>NRCH<sub>3</sub></sub>				
X	Y		λ (mμ)	lg ε	λ (mμ)	lg ε (f)	b <sub>1u</sub> <sup>2</sup> (lg ε 3.0) (Å)	λ (mμ)	lg ε	b <sub>1u</sub> <sup>2</sup> (Å)	λ (mμ)	lg ε	b <sub>1u</sub> <sup>2</sup> (Å)	λ (mμ)	lg ε	b <sub>1u</sub> <sup>2</sup> (Å)			
H	II	h d e et csa dsa	—	—	—	—	—	294	3.38	320	—	—	—	—	244	4.13	220		
			—	—	—	—	—	—	298	3.32	350	—	—	—	248	4.05	240		
			—	—	—	—	—	—	296	3.22	—	—	—	—	246	4.01	—		
			317	1.77	—	—	—	—	298	3.32	360	—	—	—	248	4.05	200		
			—	—	—	—	—	—	254	0.96	260	—	—	—	—	—	—		
NO <sub>2</sub> o	II	h d e et csa dsa	490	2.35	410	4.19 (0.30)	730 (1190)	—	—	240	—	—	—	—	—	—	—		
			—	—	425	3.73	760	—	—	—	—	—	—	—	—	—	—		
			520	2.25	425	3.84 (0.13)	750 (1370)	—	—	—	—	—	—	—	—	—	—		
			520	2.38	430	3.93	750	—	—	—	—	—	—	—	—	—	—	—	
			380	2.38	—	—	—	—	—	—	—	—	—	—	—	—	—	—	
NO <sub>2</sub> m	II	h d e et csa dsa	510	2.35	430	3.04	880	—	—	—	—	—	—	—	—	—	—		
			420	2.55	360	3.35 (0.05)	680 (330)	—	—	—	—	—	—	—	—	—	—	—	
			—	—	390	3.19	880	—	—	—	—	—	—	—	—	—	—	—	
			500	2.27	395	3.25 (0.05)	900 (830)	—	—	—	—	—	—	—	—	—	—	—	
			500	2.0	400	3.25	890	—	—	—	—	—	—	—	—	—	—	—	
NO <sub>2</sub> p	II	h d e et csa dsa	—	—	390	—	—	—	—	—	—	—	—	—	—	—	—		
			330	1.28	390	1.05	—	—	—	—	—	—	—	—	—	—	—	—	
			—	—	335	4.42 (0.51)	460 (1030)	—	—	—	—	—	—	—	—	—	—	—	
			—	—	375	4.34	470	—	—	—	—	—	—	—	—	—	—	—	—
			470	2.45	385	4.04 (0.33)	530 (1180)	—	—	—	—	—	—	—	—	—	—	—	—
		h d e et csa dsa	540	2.10	400	4.34	750	—	—	—	—	—	—	—	—	—	—		
			—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
			460	2.32	390	3.05	780	—	—	—	—	—	—	—	—	—	—	—	—
			—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
			—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—

TABLE 1 (continued)

Compound		Solvent	Longwave Inflection	Bands				$B_{C_6H_5NRCH_3}$			
X	Y			$\lambda$		$\lambda$		$\lambda$		$\lambda$	
			$\sim\lambda$ (m $\mu$ )	lg $\epsilon$	$b_{\lambda}^{m,2}$ ( $\lambda$ )	lg $\epsilon$	$b_{\lambda}^{m,2}$ ( $\lambda$ )	lg $\epsilon$	$b_{\lambda}^{m,2}$ ( $\lambda$ )	lg $\epsilon$	$b_{\lambda}^{m,2}$ ( $\lambda$ )
H	ClH <sub>3</sub>	h d e et csa dsa	—	—	—	3.36	360	—	—	254	4.19
			—	—	—	2.96	350	—	—	256	3.74
			—	—	—	3.35	350	—	—	251	4.16
			—	—	—	3.38	340	—	—	250	4.16
			322	1.69	—	2.29	260	—	—	—	—
NO <sub>2</sub> -o	CH <sub>3</sub>	h d e et csa dsa	360	1.37	—	1.67	350	—	—	—	—
			450	2.60	—	—	—	—	—	244	4.22
			—	—	790 (700)	—	—	3.64	—	—	—
			—	—	960	—	—	3.65	—	246	4.38
			510	2.45	900 (880)	—	—	3.65	—	246	4.38
NO <sub>2</sub> -m	ClH <sub>3</sub>	h d e et csa dsa	340	2.32	890	—	—	3.87	550	—	—
			—	2.45	—	—	—	2.88	360	—	—
			440	2.55	3.54 (0.09)	—	—	—	—	246	4.40
			—	—	3.48	—	—	—	—	246	4.25
			520	2.40	3.58 (0.10)	—	—	4.20	—	252	4.46
NO <sub>2</sub> -p	ClH <sub>3</sub>	h d e et csa dsa	—	—	3.54	—	—	—	420	250	4.25
			—	—	2.28	—	—	3.96	360	—	—
			360	1.45	800 (370)	—	—	3.11	—	—	—
			—	—	950	—	—	—	—	—	—
			410	2.55	3.36 (0.06)	—	—	—	—	—	—
NO <sub>2</sub> -p	ClH <sub>3</sub>	h d e et csa dsa	—	—	3.10	—	—	—	—	—	—
			—	—	3.32 (0.06)	—	—	—	—	—	—
			480	2.47	3.19	—	—	—	—	234	3.96
			480	2.47	4.25 (0.36)	—	—	—	—	—	—
			480	2.42	4.34	—	—	—	—	—	—
NO <sub>2</sub> -p	ClH <sub>3</sub>	h d e et csa dsa	—	—	4.34 (0.38)	—	—	—	—	—	—
			—	—	4.40	—	—	—	—	—	—
			480	2.47	750	—	—	—	—	—	—
			480	2.42	880	—	—	—	—	—	—
			480	2.42	880	—	—	—	—	246	3.13

TABLE 2

Characteristics of the Bands and Inflections of the Absorption Curves of Disubstituted Derivatives with the Composition  $XC_6H_4N(Y)C_6H_5$ 

Compound		Solvent	Longwave inflection		A				Bands				$B_{C_6H_4N(C_6H_5)R}$			
X	Y		$\sim\lambda$ (m $\mu$ )	lg $\epsilon$	$\lambda$ (m $\mu$ )	lg $\epsilon$	$\nu_{max}$ ( $\text{cm}^{-1}$ )	$\nu_{max}$ ( $\text{cm}^{-1}$ )	$\lambda$ (m $\mu$ )	lg $\epsilon$	$\nu_{max}$ ( $\text{cm}^{-1}$ )	$\nu_{max}$ ( $\text{cm}^{-1}$ )	$\lambda$ (m $\mu$ )	lg $\epsilon$	$\nu_{max}$ ( $\text{cm}^{-1}$ )	$\nu_{max}$ ( $\text{cm}^{-1}$ )
II	II	h	—	—	—	—	—	—	—	—	—	—	—	—	—	—
		d	—	—	—	—	—	—	—	—	—	—	—	—	—	—
		e	—	—	—	—	—	—	—	—	—	—	—	—	—	—
		et	—	—	—	—	—	—	—	—	—	—	—	—	—	—
		csa	—	—	—	—	—	—	—	—	—	—	—	—	—	—
		dsa	—	—	—	—	—	—	—	—	—	—	—	—	—	—
NO <sub>2</sub> O	H	HCl	—	—	—	—	—	—	—	—	—	—	—	—	—	—
		h	550	2.94	415	4.08(0.28)	900(1750)	370	286	4.38	—	—	—	—	—	—
		d	555	2.29	420	3.98	860	320	286	4.39	—	—	—	—	—	—
		e	540	2.45	425	3.98(0.21)	770(1600)	300	286	4.49	—	—	—	—	—	—
		ac	520	2.58	425	4.15	830	340	287	4.49	—	—	—	—	—	—
		et	550	2.87	430	3.98	1000	220	256	2.59	—	—	—	—	—	—
NO <sub>2</sub> m	II	csa	345	2.45	—	—	—	—	260	4.25	—	—	—	—	—	—
		dsa	—	—	430	3.38	880	—	270	3.74	—	—	—	—	—	—
		HCl	—	—	420	3.89	800	—	262	3.66	—	—	—	—	—	—
		h	450	2.40	370	3.22(0.05)	800(670)	—	260	4.13	—	—	—	—	—	—
		d	480	2.38	400	3.22	870	—	274	4.25	—	—	—	—	—	—
		e	480	2.40	400	3.19(0.05)	990(790)	—	280	4.44	—	—	—	—	—	—
NO <sub>2</sub> m	II	ac	—	—	400	3.27	1200	—	—	—	—	—	—	—	—	—
		et	480	2.48	400	3.16	800	—	—	—	—	—	—	—	—	—
		csa	350	2.70	—	—	—	—	282	4.38	—	—	—	—	—	—
		dsa	480	1.94	400	2.59	920	—	264	4.42	—	—	—	—	—	—
		HCl	—	—	410	3.40	740	—	280	4.43	—	—	—	—	—	—
		h	—	—	—	—	—	—	230	3.88	—	—	—	—	—	—

TABLE 2 (continued)

Compound		Solvent	Longwave Inflection	A				A <sub>lg</sub> → B <sub>lg</sub>		B <sub>C<sub>6</sub>H<sub>5</sub>NO<sub>2</sub></sub>		B <sub>C<sub>6</sub>H<sub>5</sub>N(C<sub>2</sub>H<sub>5</sub>)<sub>2</sub></sub>			
X	Y			λ (mμ)	lg ε (l)	b <sub>M</sub> 2 (lg ε 3.0) (λ)	λ (mμ)	lg ε	b <sub>M</sub> 2 (Å)	λ (mμ)	lg ε	b <sub>M</sub> 2 (Å)	λ (mμ)	lg ε	b <sub>M</sub> 2 (Å)
NO <sub>2</sub> P	II	h d e ac et csa dsa HCl	425	3.12	4.19 (0.33)	510 (1380)	—	—	—	—	—	—	—	—	—
			470	2.34	4.34	660	—	—	—	—	—	—	—	—	—
			490	2.45	4.29 (0.45)	780 (1250)	—	—	—	—	—	—	—	—	—
			467	2.30	4.07	560	—	—	—	—	—	—	—	—	—
			490	4.31	3.59	360	—	—	—	—	—	—	—	—	—
II	ClI <sub>3</sub>	h d e et csa	490	4.31	3.59	360	—	—	—	—	—	—	—	—	
			470	4.16	3.80	360	—	—	—	—	—	—	—	—	
			490	2.54	3.55	750	—	—	—	—	—	—	—	—	
			500	2.28	4.40	750	—	—	—	—	—	—	—	—	
			—	—	—	—	—	—	—	—	—	—	—	—	
NO <sub>2</sub> O	ClI <sub>3</sub>	dsa HCl h d e ac et csa	330	1.76	—	—	—	—	—	—	—	—	—	—	
			500	2.39	3.54	900 (920)	—	—	—	—	—	—	—	—	
			540	2.13	3.52	960	—	—	—	—	—	—	—	—	
			511	2.27	3.44 (0.08)	1150 (800)	—	—	—	—	—	—	—	—	
			540	2.25	3.30	—	—	—	—	—	—	—	—	—	
NO <sub>2</sub> P	ClI <sub>3</sub>	h d e ac et csa dsa HCl	510	2.94	3.78	960	—	—	—	—	—	—	—	—	
			515	2.98	3.10	—	—	—	—	—	—	—	—	—	
			515	2.54	2.76	1180	—	—	—	—	—	—	—	—	
			—	—	3.76	420	—	—	—	—	—	—	—	—	
			—	—	4.29	560 (1130)	—	—	—	—	—	—	—	—	
NO <sub>2</sub> P	ClI <sub>3</sub>	h d e ac et csa dsa HCl	473	3.02	4.36	630	—	—	—	—	—	—	—	—	
			490	2.32	4.34 (0.56)	750 (1410)	—	—	—	—	—	—	—	—	
			472	2.17	4.37	700	—	—	—	—	—	—	—	—	
			490	2.97	4.38	880	—	—	—	—	—	—	—	—	
			510	3.90	4.30	680	—	—	—	—	—	—	—	—	
NO <sub>2</sub> P	ClI <sub>3</sub>	dsa HCl	510	2.45	2.65	760	—	—	—	—	—	—	—	—	
			500	2.32	4.40	860	—	—	—	—	—	—	—	—	
			—	—	—	—	—	—	—	—	—	—	—	—	
			—	—	—	—	—	—	—	—	—	—	—	—	
			—	—	—	—	—	—	—	—	—	—	—	—	

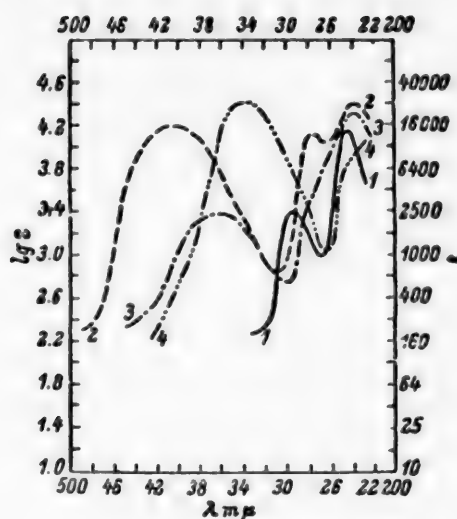


Fig. 1. Absorption spectra in hexane. 1) N-Methylaniline; 2) o-nitro-N-methylaniline; 3) m-nitro-N-methylaniline; 4) p-nitro-N-methylaniline.

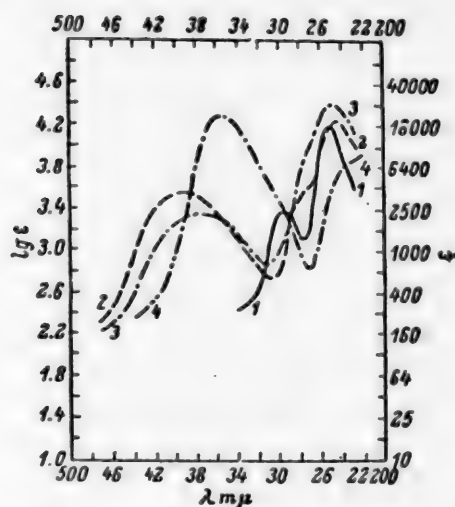


Fig. 2. Absorption spectra in hexane. 1) N-Dimethylaniline; 2) o-nitro-N-dimethylaniline; 3) m-nitro-N-dimethylaniline; 4) p-nitro-N-dimethylaniline.

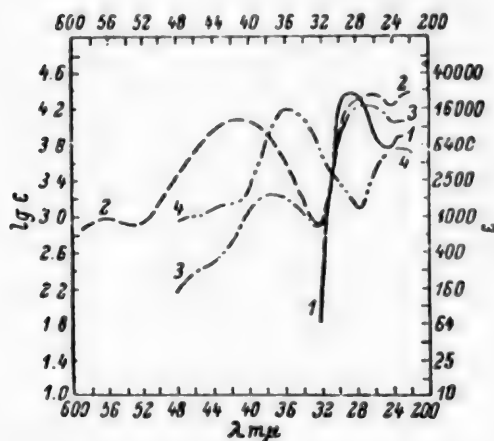


Fig. 3. Absorption spectra in hexane. 1) Diphenylamine; 2) o-nitrodiphenylamine; 3) m-nitrodiphenylamine; 4) p-nitrodiphenylamine.

of both unsubstituted and substituted benzenes (sometimes displaced somewhat toward short wavelengths) with a sharp fall in the intensity of the latter.

The shortwave bands of the monosubstituted derivatives studied, like that of aniline (at 230 mμ and  $\epsilon$  7000 in hexane), are bands not of  $A_{1g} \rightarrow B_{2u}$  electronic transitions in the ring [5], but  $N \rightarrow \pi^*$  [7] or  $\pi \rightarrow \varphi^*$  [8] transitions, accompanied by transfer of charge or optical excitation from the functional group to the ring, with the participation of the p-electrons of the amino group nitrogen in this transfer for the compounds examined. This results in the great sensitivity of this band to changes in the amino group, its absence in acid media due to binding of these p-electrons, and a number of other characteristics, which will be presented below.

The introduction of a nitro group into the ring of the monosubstituted derivatives examined produces only comparatively slight changes in the position of the band of the  $N \rightarrow \pi^*$  transitions mentioned above in-

volving the p-electrons of the NHR or  $NR_2$  groups ( $C_6H_5NRCH_3$  or  $C_6H_5NRC_6H_5$  bands). The fact that this band for the nitro derivatives has the same nature as for the starting amino compounds is demonstrated by its absence when salts are formed (in concentrated sulfuric acid). The band (or inflection) between 260 and 280 mμ, which is observed for all nitro derivatives studied, cannot be regarded as the band of  $A_{1g} \rightarrow B_{2u}$  transitions of monosubstituted derivatives displaced toward short wavelengths as it has somewhat different characteristics, namely: a) It is displaced appreciably toward long wavelengths with a change from nonpolar to polar solvents (by 6-13 mμ with a change from hexane to ethanol); b) in concentrated sulfuric acid where there is salt formation it remains and in some cases the intensity is even increased. These characteristics indicate that this band is a charge-transfer band; too, more specifically, because it occurs with nitroanilines [2] and other nitro compounds, including unsubstituted nitrobenzene (in hexane at 252 mμ and  $\epsilon$  10,000 and in ethanol at 260 mμ and  $\epsilon$  8240) [9], the band of  $N \rightarrow \pi^*$  transitions involving  $\pi$ -electrons of the nitro group and the benzene ring [10, 11] ( $C_6H_5NO_2$



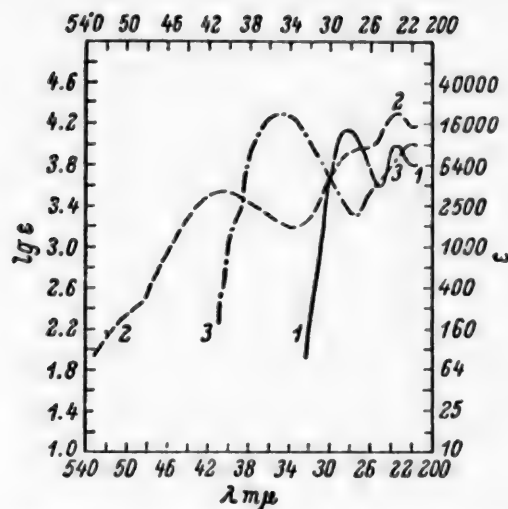


Fig. 4. Absorption spectra in hexane. 1) N-Methyldiphenylamine; 2) o-nitro-N-methyldiphenylamine; 3) p-nitro-N-methyldiphenylamine.

of this band; for para isomers, which should show the greatest change in dipole moment with this type of charge transfer, the intensity of this band is greatest, and its oscillation strength exceeds that of the meta isomer by a factor of 4-10; it is least for the meta isomer, where the possibility of this charge transfer is almost absent in the ground state. The band examined is also affected strongly by the steric effect [12] produced by departure of the functional groups from coplanarity and hence a reduction in the intensity of charge transfer involving electrons of these groups. Thus,  $(\epsilon_o/\epsilon_p)$  (in hexane) for band A for nitromethylanilines and nitrodiphenylamines is 0.58 and 0.77, while for nitrodiphenylamines it is 0.20 and 0.18, respectively. All this emphasizes the more so the characteristic of the band examined, namely that for all B bands (bands of charge transfer involving electrons of only one of the functional groups) the intensity for the para isomers is, on the contrary, less than for meta and ortho isomers. The more considerable increase in the polarity of the molecule in the excited state with the simultaneous participation of the electron-donor and electron-acceptor groups in the charge transfer also leads to a considerable increase in the effect of polar solvents in displacing the corresponding band toward long wavelengths, with the displacement reaching 25-50 mμ for the compounds examined and being especially large for precisely the para isomer. Moreover, this band disappears or is sharply reduced in intensity in media in which complete or partial salt formation is possible with binding of the p-electron of the amino group nitrogen and consequently elimination of this interaction of the substituents both in the ground and excited states for all or part of the molecules. The given nature of this band may explain its considerable width, which is produced by a decrease in the lifetime of the molecule in the excited state due to rapid transfer of the absorbed light quantum along the conjugation chain and hence the possibility of rapid nonradiative scattering of the excitation energy.

The absorption curve of a substituted nitrobenzene has a low-intensity, longwave inflection (at  $\lambda$  330 mμ and  $\epsilon$  250 in isooctane and  $\lambda$  345 mμ and  $\epsilon$  8000 in concentrated sulfuric acid [1]), which is usually ascribed to  $p \rightarrow \pi^*$  transitions localized in the nitro group [13]. All the nitro compounds studied also show a more or less clearly expressed, low-intensity, longwave inflection. However, it is at appreciably longer wavelengths than for nitrobenzene (at 420-550 mμ) and does not have many of the characteristics normally attributed to  $p \rightarrow \pi$  transitions [13, 14]. Thus, the wavelength of the inflection depends on the relative position of the substituents (Table 3) and also on the possibility of the effect on the ring of the p-electrons of the amino group; in concentrated sulfuric acid, the inflection considered is either absent or replaced by another which occupies almost the same position as that of unsubstituted nitrobenzene in sulfuric acid. Moreover, in polar solvents this inflection is displaced not toward short, but long wavelengths (Table 3), and this occurs in nonpolar dioxane in the case of nitrodiphenylamines and nitro-N-methyldiphenylamines and consequently cannot be simply the effect of complex formation due to hydrogen bonds [13]. The inflection examined (and possibly the inflection

band). The closeness of this band to the band of  $A_{1g} \rightarrow B_{2u}$  transitions in the ring may lead to their superposition, which explains its slight displacement toward long wavelengths in nitroanilines in comparison with nitrobenzene.

With all the nitroanilines studied, the absorption curve showed a new, intense (in hexane  $\log \epsilon_{\max}$  3.2-4.4), extremely wide [as a rule,  $b(\epsilon_m/2)$  varied between 500 and 900 Å], and almost symmetrical band with a maximum between 350 and 430 mμ, which was absent from the curves of monosubstituted derivatives. As was shown previously [2, 10], this type of band (band A) is characteristic only of disubstituted derivatives containing functional groups with opposite electrical conjugation effects, and in origin it corresponds to bands of charge transfer involving p- and  $\pi$ -electrons of the two functional groups, i.e., electron-donor and electron-acceptor groups. This is indicated by the fact that this band depends considerably on the relative position of the substituents with  $\lambda_{\max(o-)} - \lambda_{\max(p-)}$  reaching 75 mμ, while for B bands, the difference in the position of the maxima for isomers reaches a maximum of 20 mμ and is generally less than 10 mμ. The relative position of the substituents has a particularly strong effect on the intensity

TABLE 3

Relations of  $\lambda$  ( $\Delta\lambda$  in m $\mu$ ),  $f$  and  $b$  of isomers in Hexane

Compound	Band A						Longwave inflection					
	$\lambda_{o-o}$	$\lambda_{m-m}$	$\lambda_{o-p}$	$f_{m-}$	$f_{p-}$	$b_{m-}/b_{p-}$	$\lambda_{e-h}$			$\lambda_{e-h}$		
	$\lambda_{o-o}$	$\lambda_{m-m}$	$\lambda_{o-p}$	$f_{m-}$	$f_{p-}$	$b_{m-}/b_{p-}$	o-	m-	p-	o-	m-	p-
$C_6H_4(NO_2)NHCH_3$	-50	-	-75	6.0	0.58	3.6	+15	+35	+50	+30	+80	+70
$C_6H_4(NO_2)NHC_6H_5$	+45	-	+65	5.6	0.85	(2.6)	+10	+30	+50	+10	+30	+100
$C_6H_4(NO_2)N(CH_3)_2$	+20	-	+40	1.5	0.40	1.62	+25	+25	+40	+60	+80	+10
$C_6H_4(NO_2)N(CH_3)C_6H_5$	-	-	+58	-	0.16	-	+5	-	+38	+40	-	-

of unsubstituted nitrobenzene) is evidently connected not with  $p \rightarrow \pi^*$ , but  $\pi \rightarrow \pi^*$  transitions [8, 15], which are also localized in the nitro group.

The data obtained for absorption in concentrated and dilute acids indicate the strength of the salts formed by various nitro compounds. Thus, from these data it follows that there is hardly any salt formation with nitrodiphenylamines and nitro-N-methyldiphenylamines, especially in HCl-saturated ethanol, and that with the latter (and possibly p-nitrodiphenylamine) the tendency for salt formation is sharply reduced in concentrated sulfuric acid. Evidently depending on the basicity of the starting nitro amino compound, in dilute acids there is complete or partial (reduction in intensity) restoration of the curve in ethanol or water. In some cases (with m-nitromethylaniline and o-nitrodiphenylamine) the curve then partly shows both bands of nitrobenzene and also bands of nitro amino compounds with an appreciable reduction in their intensity.

o-Nitromethylaniline and o-nitrodiphenylamine are compounds which, as was pointed out above, are considered to have an intramolecular hydrogen bond, and in contrast to o-nitrodiphenylamine and o-nitro-N-methyldiphenylamine, they show the same absorption characteristics as other compounds with this type of bond. As follows from the data in Table 3, band A of o-nitromethylaniline and o-nitrodiphenylamine is displaced toward long wavelengths in comparison with that of the isomers, is appreciably widened, and has quite a high oscillation strength (close to that of the para isomer). Band A of these compounds also undergoes an appreciably smaller displacement toward long wavelengths than with the isomers when the hydrocarbon solvent is replaced by a hydroxyl-containing solvent. The presence of an intramolecular hydrogen bond also apparently has an appreciable effect on the longwave inflection as the latter shows most of the characteristics given for band A. The peculiarity of the ortho compounds examined is shown by the fact that with  $C_6H_4(NO_2)N(CH_3)R$  as compared with  $C_6H_4(NO_2)NHR$ , in the case of the ortho isomers there is a displacement of the longwave inflection and band A toward short wavelengths, and in the case of the meta and para isomers, on the contrary, there is a displacement toward long wavelengths. With the former there is a sharp fall in the oscillation strength and narrowing, while these characteristics of band A remain almost unchanged with the meta and para isomers. These characteristics of the effect of the intramolecular hydrogen bond indicate the higher strength of this bond in the excited state than in the ground state [16], which evidently promotes to a particularly large extent during excitation the charge transfer involving both the electron-donor and electron-acceptor groups. Therefore, the intramolecular hydrogen bond has a considerable effect on band A and an appreciably smaller effect on the other absorption bands of the compounds examined.

#### SUMMARY

1. The absorption curves of N-methylaniline, N,N-dimethylaniline, diphenylamine, and N-methyldiphenylamine and their ortho-, meta-, and para-nitro derivatives in various solvents were measured.

It was shown that their absorption bands may be ascribed to  $A_{1g} \rightarrow B_{2u}$  transitions in the ring,  $N \rightarrow \pi$  transitions with charge transfer from the ring to the substituent or, on the other hand, from one functional group to another, and also to  $p \rightarrow \pi^*$  (or  $\pi \rightarrow \pi^*$ ) transitions localized in the nitro group.

2. The characteristics of the absorption of o-nitromethylaniline and o-nitrodiphenylamine confirm that these molecules contain an intramolecular hydrogen bond.

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## INTRAMOLECULAR HYDROGEN BOND AND ULTRAVIOLET ABSORPTION SPECTRA

### IX. NITROACETANILIDES AND NITRO-N-ACETYLDIPHENYLAMINES

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The electronic spectra of nitroacetanilides and nitro-N-acetyldiphenylamines are of interest in connection with the elucidation of the nature of electronic transitions connected with the different absorption bands and also in connection with the determination of the effect of an intramolecular hydrogen bond on absorption. The presence of the latter in o-nitroacetanilide follows from its dipole moment [1], electrochemical behavior [2], and absorption in ethanol [3]. We used an SF-4 spectrophotometer to measure the absorption of acetanilide and N-acetyldiphenylamine and their ortho-, meta-, and para-nitro derivatives in the following solvents: hexane (h) (apart from the insoluble m- and p-nitroacetanilides), dioxane (d), ethanol (e), 2 N ethanol solution of sodium alcoholate (et), concentrated (98%) sulfuric acid (csa), dilute (9.8%) sulfuric acid (dsa), and ethanol saturated with gaseous HCl (HCl). Some of the absorption curves are given in Figs. 1-5 and the others were given in [4]. The characteristics of the bands and inflections of the absorption curves, namely the wavelengths ( $\lambda$  in m $\mu$ ) of the maxima and inflections, the oscillation strength ( $f$ ) and width ( $b$ ) at  $\epsilon_m/2$  ( $\epsilon_m$  is the extinction of the maximum) or at  $\log \epsilon \ 3.0$ , are given in Table 1. The values obtained for the positions of the maxima and inflections of the bands of the substances studied in ethanol deviate from literature data [3, 5, 6, 7] only in some cases and by a maximum of  $\pm 2-3$  m $\mu$ .

In the number of bands, the absorption curves of the compounds studied were mainly the same as those of the starting compounds, namely, aniline and diphenylamine and their nitro derivatives [8, 9]. On the basis of the values of  $\epsilon_m$ , it is assumed [3] that the bands of the compounds examined are the absorption bands of benzene itself displaced toward long wavelengths, namely the bands at 220-250 m $\mu$  of acetanilide and its nitro derivatives are derived from the band of benzene 203.5 m $\mu$  ( $A_{1g} \rightarrow B_{1u}$  transitions), and the bands with a maximum at 300-350 m $\mu$  of o- and m-nitroacetanilides are derived from the band of benzene at 254 m $\mu$  ( $A_{1g} \rightarrow B_{2u}$  transitions). The band with a maximum at 316 m $\mu$  of p-nitroacetanilide belongs to the former [3]. However, even with nitro-N-acetyldiphenylamines, the position ( $\lambda_m$ ) of this band in ethanol for the meta and para isomers is the same; this type of band of para-nitro derivatives is the same in properties (width, disappearance on salt formation, etc.), as the corresponding longwave bands (at 308-350 m $\mu$ ) of the ortho- and meta-nitro derivatives. These bands likewise cannot be considered as a displaced second band of benzene at 254 m $\mu$ . This follows from the considerable dependence of the characteristics of these bands in hexane ( $\lambda_{max}$ ,  $\epsilon_{max}$ , and  $f$ ) on the relative position of the substituents, on the type of solvent (appreciable displacement toward long wavelengths in dioxane), and on the nature of the functional groups (Table 2). These characteristics indicate the different origin of the bands examined, namely their connection, as in the case of disubstituted benzenes with one electron-donor and one electron-acceptor group studied previously [8], with the transfer of charge from one functional group to the other through the  $\pi$ -electron system of the benzene ring during excitation (band A). The somewhat different effect of ethanol on these bands of the acetyl derivatives (displacement toward short rather than long wavelengths) is apparently connected with the capacity of the acetyl group to interact with ethanol

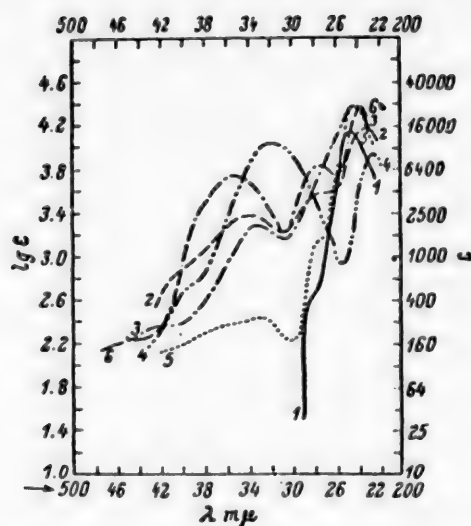


Fig. 1. Absorption spectra in ethanol. 1) N-Acetylaniline; 2) o-nitro-N-acetylaniline; 3) m-nitro-N-acetylaniline; 4) p-nitro-N-acetylaniline; 5) N-acetylaniline in hexane; 6) o-nitro-N-acetylaniline in hexane.

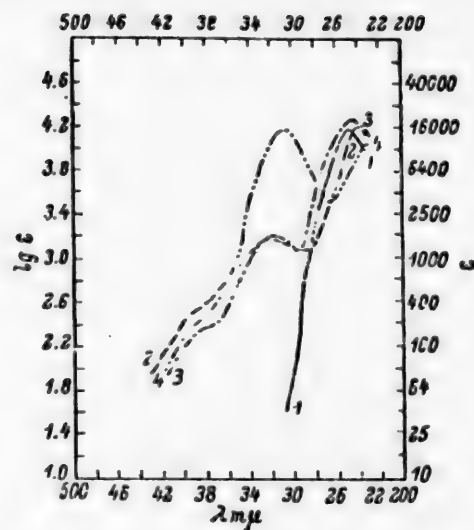


Fig. 2. Absorption spectra in hexane. 1) N-Acetyldiphenylamine; 2) o-nitro-N-acetyldiphenylamine; 3) m-nitro-N-acetyldiphenylamine; 4) p-nitro-N-acetyldiphenylamine.

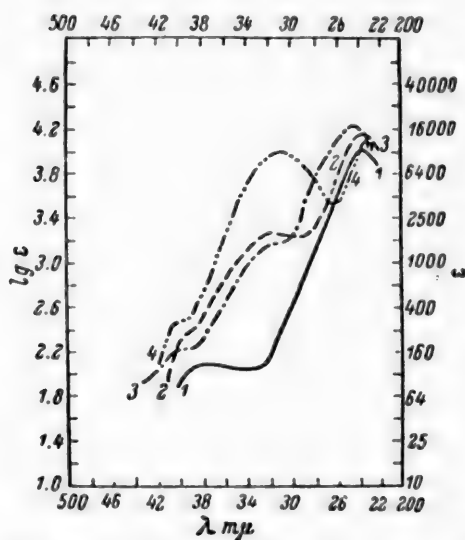


Fig. 3. Absorption spectra in ethanol. 1) N-Acetyldiphenylamine; 2) o-nitro-N-acetyldiphenylamine; 3) m-nitro-N-acetyldiphenylamine; 4) p-nitro-N-acetyldiphenylamine.

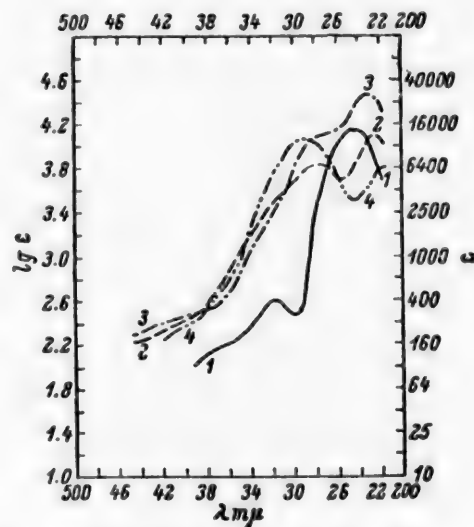


Fig. 4. Absorption spectra in conc.  $H_2SO_4$ . 1) N-Acetylaniline; 2) o-nitro-N-acetylaniline; 3) m-nitro-N-acetylaniline; 4) p-nitro-N-acetylaniline.

molecules. The appreciable sensitivity to the nature of the functional group, like the disappearance (or reduction in  $\epsilon_m$ ) on salt formation, indicates that the shortwave band is not a band of electronic transitions localized in the ring, but a band of charge transfer involving p-electrons of the nitrogen of the amino groups (band B).

The introduction of an N-acetyl group into the starting amino or N-phenylamino derivatives of benzene produces (Table 2) [3, 9-11] a sharp displacement of the longwave inflection and band A toward short wavelengths with an appreciable reduction in both the width and oscillation strength of the latter. The B bands are



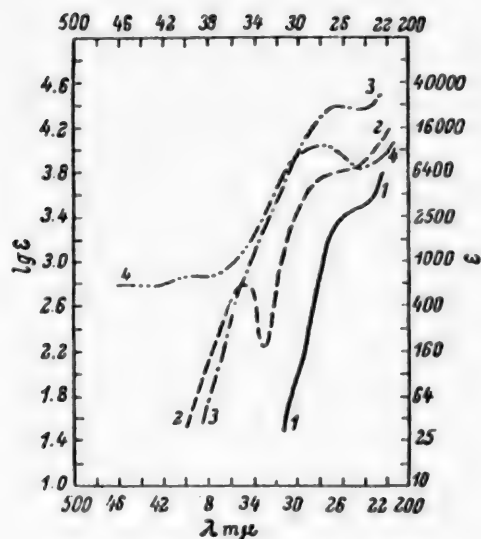


Fig. 5. Absorption spectra in conc.  $H_2SO_4$ . 1) N-Acetyldiphenylamine; 2) o-nitro-N-acetyldiphenylamine; 3) m-nitro-N-acetyldiphenylamine; 4) p-nitro-N-acetyldiphenylamine.

In the case of salt formation involving the p-electrons of the amino group, the absorption curve of the compounds examined must undergo a substantial change, and in the case of monosubstituted derivatives it must approach that of benzene, while with nitro amines it must approach that of nitrobenzene. In actual fact, in concentrated sulfuric acid the absorption curve of all the nitro compounds studied is displaced toward short wavelengths and consists, as in the case of nitrobenzene in this medium [13], of a longwave, low-intensity inflection between 350 and 390  $m\mu$  ( $\log \epsilon$  2.5-2.9) and a band in the region of 268-290  $m\mu$  ( $\log \epsilon$  3.8-4.3) (for nitrobenzene the inflection is at  $\sim 345$   $m\mu$  with  $\log \epsilon$  2.9 and the band at 286  $m\mu$  with  $\log \epsilon$  4.03). Band A is absent from the curve; in most cases the band  $BC_6H_5NHC(=O)CH_3$  is also absent. In dilute sulfuric acid there is only partial salt formation, as follows from the appearance on the curve of the same absorption bands as in hexane but with an appreciably lower intensity. In the case of o-nitroacetanilide in dilute sulfuric acid, as in sodium ethanolate, there is the possibility of elimination of the acetyl group. In the case of nitro-N-acetyldiphenylamines in an ethanol solution of HCl of the concentration used, salt formation is evidently completely absent since the absorption curve in this medium is the same as that in ethanol with respect to  $\epsilon_{max}$ . The same follows for the monosubstituted derivatives examined in concentrated sulfuric acid, where salt formation is apparently almost absent [14].

o-Nitroacetanilide shows a series of spectral peculiarities in comparison with its isomers. Thus, the maximum of band A of o-nitroacetanilide is appreciably displaced toward long wavelengths in comparison with the meta and para isomers and to a considerably greater extent than for o-nitro-N-acetyldiphenylamine; the oscillation strength of this band of o-nitroacetanilide is greater than that of the meta isomer, while those of nitro-N-acetyldiphenylamines are comparable with each other; band A of o-nitroacetanilide is wider than that of the para isomer; in ethanol as compared with hexane, this band is displaced toward short wavelengths to a considerably greater extent than for the isomers (meta-), while for nitro-N-acetyldiphenylamines, it is displaced in the same direction to the same extent for all the isomers.

With the replacement of hydrogen of nitroacetanilides by a phenyl group, in the ortho isomer there is a sharp displacement of band A toward short wavelengths, while with the para isomer the position of this band is completely unchanged (Table 3). As was shown previously [8, 9, 10, 15], all these relations are characteristic of compounds with an intramolecular hydrogen bond in the ortho isomer; evidently as a result of the characteristics of the N-acetyl group, the effect of this type of bond in nitroacetanilides appears less sharply than in nitromethylanilines and nitrodiphenylamines, for example (see [9]).

then displaced to a considerably smaller extent and, on the contrary, generally toward long wavelengths. The acetyl group at the amino group nitrogen reduces the tendency of the p-electrons of this atom for displacement to the ring. The presence of this group evidently decreases the interaction of the functional groups to a different extent in the ground and excited states so that the difference in the energy levels for charge transfer from one function group to the other increases, while that for charge transfer from the amino group to the ring decreases in most cases.

From the data in Table 1 it follows that in 2 N sodium ethanolate the absorption curves of all the compounds investigated, especially the nitro derivatives, undergo substantial changes. In number and position ( $\lambda_m$  and  $\epsilon_m$ ) of the bands, the curves are identical with those of the compounds without an acetyl group, i.e., in the case of acetanilide and its nitro derivatives, identical to the curve of aniline and its nitro derivatives in ethanol [8, 6], and in the case of N-acetyldiphenylamine and its nitro derivatives, identical to those of diphenylamine and nitrodiphenylamines in ethanol or sodium ethanolate [9]. The acetyl compounds studied evidently undergo almost complete alcoholysis in ethanolate solution, and this agrees with their normal behavior in the medium examined [12].



TABLE 1

Characteristics of Bands and Inflections of Absorption Curves of Compounds with the Composition  $\text{XC}_6\text{H}_4\text{N}(\text{COCH}_3)\text{Y}$ 

Compound		Solvent	Longwave Inflection		A				Bands				$\text{H}_2\text{C}_6\text{H}_4\text{NO}_2$		$\text{H}_2\text{C}_6\text{H}_4\text{N}(\text{COCH}_3)\text{H}$	
X	Y		$\lambda_{\text{inf}}$ (m $\mu$ )	lg $\epsilon$	$\lambda_{\text{M}}$ (m $\mu$ )	lg $\epsilon_{\text{M}}$ (l)	$b_{\text{M}}^2$ (lg $\epsilon$ 3.0) ( $\text{\AA}$ )	$\lambda_{\text{M}}$ (m $\mu$ )	lg $\epsilon_{\text{M}}$	$b_{\text{M}}^2$ ( $\text{\AA}$ )	$\lambda_{\text{M}}$ (m $\mu$ )	lg $\epsilon_{\text{M}}$	$b_{\text{M}}^2$ ( $\text{\AA}$ )	$\lambda_{\text{M}}$ (m $\mu$ )	lg $\epsilon_{\text{M}}$	$b_{\text{M}}^2$ ( $\text{\AA}$ )
II	II	h	330	2.43	—	—	—	—	—	—	—	—	—	—	—	—
		d	—	—	—	—	—	—	—	—	—	—	—	—	—	—
		e	—	—	—	—	—	—	—	—	—	—	—	—	—	—
		et	—	—	—	—	—	—	—	—	—	—	—	—	—	—
NO <sub>2</sub> -o	II	csa	320	2.59	—	—	—	—	—	—	—	—	—	—	—	—
		dsa	370	1.54	—	—	—	—	—	—	—	—	—	—	—	—
		h	420	2.35	350	3.74 (0.13)	570 (760)	—	—	—	—	—	—	—	—	—
		d	—	—	355	3.51	700	—	—	—	—	—	—	—	—	—
NO <sub>2</sub> -m	II	e	400	2.88	340	3.38 (0.07)	—	—	—	—	—	—	—	—	—	—
		et	—	—	410	3.72	800	—	—	—	—	—	—	—	—	—
		csa	380	2.56	—	—	—	—	—	—	—	—	—	—	—	—
		dsa	500	1.22	408	2.47	800	—	—	—	—	—	—	—	—	—
NO <sub>2</sub> -p	II	d	—	—	330	3.30	—	—	—	—	—	—	—	—	—	—
		e	400	2.38	328	3.29 (0.05)	—	—	—	—	—	—	—	—	—	—
		et	—	—	360	2.99	—	—	—	—	—	—	—	—	—	—
		csa	367	2.59	—	—	—	—	—	—	—	—	—	—	—	—
NO <sub>2</sub> -p	H	dsa	410	1.48	325	2.22	—	—	—	—	—	—	—	—	—	—
		d	—	—	316	4.12	580	—	—	—	—	—	—	—	—	—
		e	380	2.85	318	4.04 (0.30)	530 (920)	—	—	—	—	—	—	—	—	—
		et	—	—	380	3.82	920	—	—	—	—	—	—	—	—	—
NO <sub>2</sub> -p	H	csa	370	2.58	—	—	—	—	—	—	—	—	—	—	—	—
		dsa	430	1.57	318	3.02	580	—	—	—	—	—	—	—	—	—



TABLE 2

$$\Delta\lambda \text{ (m}\mu\text{)} = \lambda_{\text{XC}_6\text{H}_4\text{N(Y)COCH}_3} - \lambda_{\text{XC}_6\text{H}_4\text{N(Y)H}}$$

X	Solvent	Y = H			Y = C <sub>6</sub> H <sub>5</sub>		
		longwave inflection	bands		longwave inflection	bands	
			A	B <sub>C<sub>6</sub>H<sub>5</sub>NHCOCH<sub>3</sub></sub>		A	B <sub>C<sub>6</sub>H<sub>5</sub>NHCOCH<sub>3</sub></sub>
H	h	—	—	+12	—	—	+20
NO <sub>2</sub> -o	h	—	—	—	-167	-95	+14
NO <sub>2</sub> -m	h	-76	-65	-1	-155	-105	+10
NO <sub>2</sub> -p	h	—	—	—	-80	-52	+12
NO <sub>2</sub> -p	e	-60	-47	+9	-95	-90	—
COCH <sub>3</sub> -o	h	—	—	-6	-41	-42	-4
COCH <sub>3</sub> -o	e	-65	-54	-6	-94	-90	—
COCH <sub>3</sub> -m	h	—	-24	+6	—	—	—
COCH <sub>3</sub> -m	e	—	-35	+3	—	—	—
COCH <sub>3</sub> -o	h	—	-24.5	+6.5	—	—	—
COCH <sub>3</sub> -o	e	—	-29	+5.0	—	—	—
COOH-o	h	—	-12.5	—	—	—	—
COOH-o	e	—	-27.5	—	—	—	—
COOH-m	h	—	-27	+5	—	—	—
COOH-m	e	—	-24	+4	—	—	—
COOH-p	e	—	-18	—	—	—	—

TABLE 3

Relations of  $\lambda$  ( $\Delta\lambda$  in m $\mu$ ) and  $f$  for Bands A of Isomers

	Solvent	$\lambda_o - \lambda_m$	$\lambda_o - \lambda_p$	$\frac{f_o}{f_m}$	$\epsilon - \lambda d$			$\lambda_{\text{N(C}_6\text{H}_5\text{)COCH}_3} - \lambda_{\text{NHCOCH}_3}$		
					o-	m-	p-	o-	m-	p-
C <sub>6</sub> H <sub>4</sub> (NO <sub>2</sub> )NHCOCH <sub>3</sub>	d	+20	+39	1.4 (a)	-15	-2	+2	-28	-10	0
C <sub>6</sub> H <sub>4</sub> (NO <sub>2</sub> )N(C <sub>6</sub> H <sub>5</sub> )COCH <sub>3</sub>	h	+2	+12	1.0	-7	-10	-6	—	—	—
	d	+7	+11	—	—	—	—	—	—	—

## SUMMARY

1. On the basis of data on the visible and ultraviolet absorption of acetanilide, N-acetyldiphenylamine, and their ortho-, meta-, and para-nitro derivatives in various solvents it was established that the introduction of an N-acetyl group produces a considerable displacement of the longwave inflection and the longwave band (A) toward short wavelengths, while, on the contrary, the shortwave band (B) is generally displaced toward long wavelengths; the effect of various polar solvents on the position of the absorption bands is appreciably reduced with acetyl compounds.

2. Nitroacetanilides and nitro-N-diphenylamines undergo almost complete alcoholysis in 2 N ethanol solution of sodium alcoholate; the introduction of a nitro group into acetanilide and N-acetyldiphenylamines increases the tendency of the N-acetyl group to participate in salt formation in concentrated and dilute sulfuric acid.

3. o-Nitroacetanilide shows the same spectral characteristics as other compounds with an intramolecular hydrogen bond.

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## ELECTRONIC SPECTRA OF AROMATIC NITROSOAMINES

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For elucidating the character of the reaction of the unshared p-electrons of an N-nitrosoamino group nitrogen with the  $\pi$ -electronic system of aromatic rings [1] we measured the absorption in the region of 2200-7000 Å (on an SF-4 spectrophotometer) of N-nitroso-N-methylaniline and N-nitrosodiphenylamine and their ortho-, meta-, and para-nitro derivatives in the following solvents: hexane (h), ethanol (e), dioxane (d), 2 N alcohol solution of sodium alcoholate (et), concentrated (98%) sulfuric acid (csa), and dilute (9.8%) aqueous sulfuric acid (dsa) and also ethanol saturated with gaseous HCl (HCl) in the case of N-nitrosodiphenylamines. The synthesis and purification of the substances studied have been given previously [2, 3]; a detailed description of the measurement procedure and purification of the solvents was given in [3]. Absorption curves in hexane, ethanol, and concentrated sulfuric acid are given in Figs. 1-5; the others are given in [3]. The characteristics of the bands and absorption curves of the compounds examined ( $\lambda_m$  in m $\mu$  for the maxima and inflections,  $\log \epsilon_m$ , and  $b\epsilon_m/2$ , i.e., the width at  $\epsilon_{max}/2$ ) are given in the table.

A comparison with the absorption curves of N-methylaniline and diphenylamine in hexane shows that the introduction of a nitroso group produces the following effects: a) for the former a displacement toward short wavelengths of the band of  $A_{1g} \rightarrow B_{2u}$  electronic transitions and band B, which is connected with charge transfer involving the p-electrons of the amino group nitrogen, while for the latter, on the contrary, they show some displacement toward long wavelengths; b) the appearance of a low-intensity inflection in the longwave region in some cases. The displacement of this inflection toward short wavelengths in ethanol as compared with hexane indicates its connection with  $p \rightarrow \pi^*$  transitions in the nitroso group itself.

In comparison with the curves of nitro-N-methylanilines and nitrodiphenylamines, the absorption curves of the nitro derivatives are appreciably displaced toward short wavelengths and undergo substantial changes. The ortho and meta isomers do not show band A, which is connected with charge transfer involving  $\pi$ - and p-electrons of the two functional groups during optical excitation; the para isomers show this band with its maximum displaced toward short wavelengths in comparison with that of the starting materials by 29 and 35 m $\mu$ , respectively; with all the nitro derivatives, the low-intensity, longwave inflection is at appreciably shorter wavelengths (by 40-100 m $\mu$ ) than with the starting secondary amines. The presence of band A in the case of p-nitro-N-nitrosoamines and also band  $B_{C_6H_5NHR}$  in the case of all the compounds studied indicates that the introduction of an NO group into a secondary aromatic amine does not change the electronic nature of the NHR group. There is only a reduction in the activity of its interaction with an NO<sub>2</sub> group in the ortho and meta positions, as a result of which the band A does not appear clearly in the case of o- and m-nitro-N-nitroso compounds, though its presence is indicated by the considerable drawing out of the longwave edge of the absorption curve, especially with nitrodiphenylamines (Figs. 1 and 2).

In an ethanol solution of sodium alcoholate, the absorption curves of all the nitroso compounds studied, apart from nitro-N-nitrosodiphenylamines, remained basically the same as in ethanol. Only with the latter was there a substantial change in the absorption curves, namely the appearance of band A, and with the meta and ortho isomers, a substantial displacement of the longwave inflection toward long wavelengths. With respect to

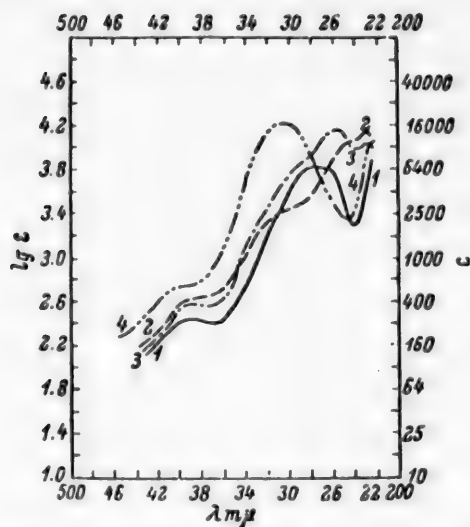


Fig. 1. Absorption spectra in hexane. 1) N-Methylnitrosoaniline; 2) o-nitro-N-methylnitrosoaniline; 3) m-nitro-N-methylnitrosoaniline; 4) p-nitro-N-methylnitrosoaniline.

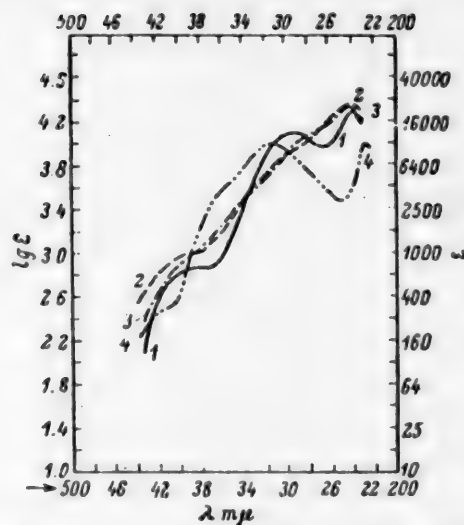


Fig. 2. Absorption spectra in hexane. 1) N-Nitrosodiphenylamine; 2) o-nitro-N-nitrosodiphenylamine; 3) m-nitro-N-nitrosodiphenylamine; 4) p-nitro-N-nitrosodiphenylamine.

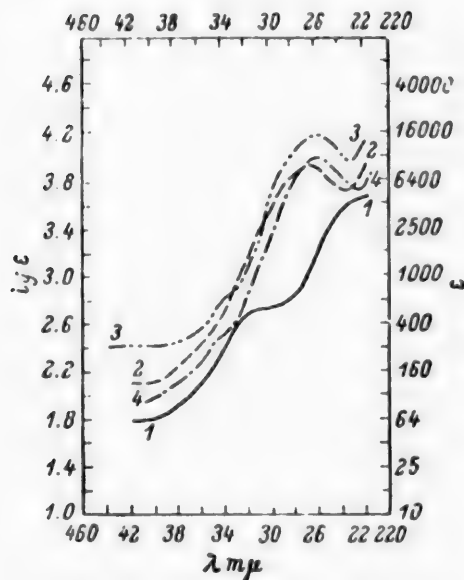


Fig. 3. Absorption spectra in conc.  $H_2SO_4$ . 1) N-Methylnitrosoaniline; 2) o-nitro-N-methylnitrosoaniline; 3) m-nitro-N-methylnitrosoaniline; 4) p-nitro-N-methylnitrosoaniline.

the position of the bands and inflections, the absorption curves of all the nitro-N-nitrosodiphenylamines in ethanolate are very similar to those of the corresponding nitrodiphenylamines in this medium and in neutral solvents in general [4]. It is evident that in 2 N ethanol solution of sodium ethanolate the effect of the nitroso group in the compounds examined is almost absent, and, as in the case of acetyl derivatives [5], this may be caused by elimination of the nitroso group.

The absorption curves of the nitro derivatives (apart from o- and p-nitro-N-nitrosodiphenylamines) in concentrated sulfuric acid consist of an inflection and band with almost the same values of  $\lambda$  and  $\epsilon$  as for unsubstituted nitrobenzene in this medium, namely an inflection between 330 and 350  $m\mu$  (at  $\sim 345 m\mu$  for nitrobenzene) and a band between 258 and 270  $m\mu$  (at 286  $m\mu$  for nitrobenzene). With o- and p-nitro-N-nitrosodiphenylamines, the presence of concentrated sulfuric acid produces a displacement of the curve toward long wavelengths with strong development of the absorption in the region of the longwave inflection to form a band with a maximum at  $\lambda$  of 540-550  $m\mu$ .

The development of this band in concentrated sulfuric acid is apparently common to all ortho- and para- (apart from o-nitrodiphenylamine, which has an intramolecular hydrogen bond), but not meta-nitro derivatives of diphenylamine since it is observed with p-nitrodiphenylamine, o- and p-nitro-N-methyldiphenylamines, etc. The appearance of this band is evidently connected, on the one hand, with the possibility of strong interaction of the groups in the molecule and the presence of the diphenylamino group and, on the other hand, with a specific interaction of the nitro (or nitroso) groups with acid molecules. That this is connected with an interaction with the nitroso group follows from the fact that in





(continued)

Compound		Solvent	Bands														
X	Y		Longwave Infection		A			A <sub>lg</sub> → B <sub>lg</sub>			B <sub>C<sub>6</sub>H<sub>5</sub>NO<sub>2</sub></sub>			B <sub>C<sub>6</sub>H<sub>5</sub>N(NO)(C<sub>6</sub>H<sub>5</sub>)</sub>			
			$\lambda$ (m $\mu$ )	lg $\epsilon$	$\lambda$ (m $\mu$ )	lg $\epsilon_M$	$\nu_{M/2}$ ( $\text{\AA}$ )	$\lambda$ (lg)	lg $\epsilon_M$	$\nu_{M/2}$ ( $\text{\AA}$ )	$\lambda$ (m $\mu$ )	lg $\epsilon_M$	$\nu_{M/2}$ ( $\text{\AA}$ )	$\lambda$ (m $\mu$ )	lg $\epsilon_M$	$\nu_{M/2}$ ( $\text{\AA}$ )	
H	C <sub>6</sub> H <sub>5</sub>	h	375	2.88	—	—	—	—	—	—	—	—	—	—	—	—	—
		d	390	2.80	—	—	—	—	—	—	—	—	—	—	—	—	—
		e	367	2.05	—	—	—	—	—	—	—	—	—	—	—	—	—
		et	380	2.36	—	—	—	—	—	—	—	—	—	—	—	—	—
		csa	620	3.46	—	—	—	—	—	—	—	—	—	—	—	—	—
NO <sub>2</sub> -o	C <sub>6</sub> H <sub>5</sub>	dsa	420	2.88	—	—	—	—	—	—	—	—	—	—	—	—	—
		HCl	410	3.74	—	—	—	—	—	—	—	—	—	—	—	—	—
		h	390	3.00	—	—	—	—	—	—	—	—	—	—	—	—	—
		d	390	2.92	—	—	—	—	—	—	—	—	—	—	—	—	—
		e	385	2.63	—	—	—	—	—	—	—	—	—	—	—	—	—
NO <sub>2</sub> -m	C <sub>6</sub> H <sub>5</sub>	et	—	2.95	—	—	—	—	—	—	—	—	—	—	—	—	—
		csa	350	—	—	—	—	—	—	—	—	—	—	—	—	—	—
		dsa	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
		HCl	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
		h	385	3.02	—	—	—	—	—	—	—	—	—	—	—	—	—
NO <sub>2</sub> -p	C <sub>6</sub> H <sub>5</sub>	d	380	2.83	—	—	—	—	—	—	—	—	—	—	—	—	—
		e	380	2.67	—	—	—	—	—	—	—	—	—	—	—	—	—
		et	500	2.12	—	—	—	—	—	—	—	—	—	—	—	—	—
		csa	385	2.20	—	—	—	—	—	—	—	—	—	—	—	—	—
		dsa	350	2.77	—	—	—	—	—	—	—	—	—	—	—	—	—
NO <sub>2</sub> -p	C <sub>6</sub> H <sub>5</sub>	HCl	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
		h	405	2.56	—	—	—	—	—	—	—	—	—	—	—	—	—
		d	395	3.02	—	—	—	—	—	—	—	—	—	—	—	—	—
		e	395	2.90	—	—	—	—	—	—	—	—	—	—	—	—	—
		et	485	3.79	—	—	—	—	—	—	—	—	—	—	—	—	—
NO <sub>2</sub> -p	C <sub>6</sub> H <sub>5</sub>	csa	565	4.05	—	—	—	—	—	—	—	—	—	—	—	—	—
		dsa	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
		HCl	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
		h	395	3.99	—	—	—	—	—	—	—	—	—	—	—	—	—
		d	320	4.34	—	—	—	—	—	—	—	—	—	—	—	—	—
NO <sub>2</sub> -p	C <sub>6</sub> H <sub>5</sub>	e	318	4.21	—	—	—	—	—	—	—	—	—	—	—	—	—
		et	316	4.01	—	—	—	—	—	—	—	—	—	—	—	—	—
		csa	336	3.72	—	—	—	—	—	—	—	—	—	—	—	—	—
		dsa	400	3.29	—	—	—	—	—	—	—	—	—	—	—	—	—
		HCl	390	4.34	—	—	—	—	—	—	—	—	—	—	—	—	—

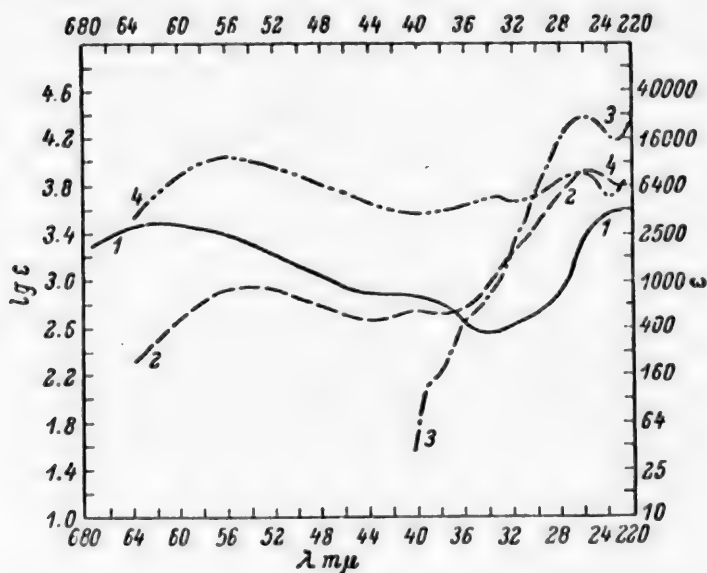


Fig. 4. Absorption spectra in conc.  $H_2SO_4$ . 1) N-Nitrosodiphenylamine; 2) o-nitro-N-nitrosodiphenylamine; 3) m-nitro-N-nitrosodiphenylamine; 4) p-nitro-N-nitrosodiphenylamine.

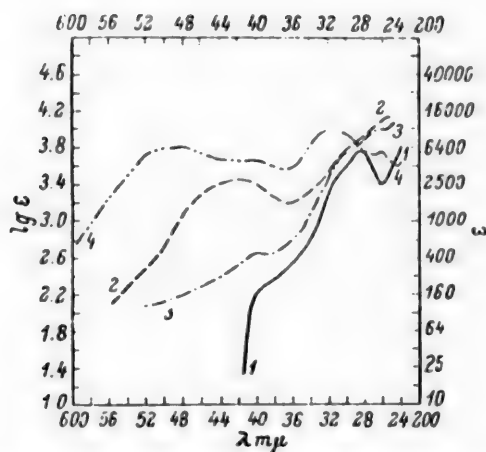


Fig. 5. Absorption spectra in sodium alcoholate. 1) N-Nitrosodiphenylamine; 2) o-nitro-N-nitrosodiphenylamine; 3) m-nitro-N-nitrosodiphenylamine; 4) p-nitro-N-nitrosodiphenylamine.

(for N-nitrosodiphenylamine) or in the appearance of bands of  $A_{1g} \rightarrow B_{2u}$  transitions of benzene ( $254 m\mu$ ) (for N-nitrosomethylaniline).

contrast to nitroso-N-methylaniline, nitrosodiphenylamine itself gives the same band in concentrated sulfuric acid, while the participation of the molecules of the former in salt formation in this medium is apparently suppressed. It is possible that the appearance of second inflections (or bands) in the region of band A ( $300-310 m\mu$ ) with unsubstituted N-nitroso compounds in concentrated and dilute sulfuric acid is produced by partial rearrangement with the formation of the corresponding p-nitroso-N-methyl(phenyl)anilines [6].

In dilute sulfuric acid and HCl, the absorption curves of all the nitro-N-nitroso compounds studied (apart from p-nitro-N-nitrosomethylaniline) were found to be almost identical with those of the corresponding compounds without the nitroso group. As in ethanol solutions of sodium alcoholate, this may be connected with the elimination of the effect of the nitroso group due to its removal or specific interaction with solvent molecules, restoring the normal effect of the amino group.

With unsubstituted N-nitroso compounds in dilute acids there is partial or almost complete salt formation, which appears as a reduction in the intensity of the bands

## SUMMARY

1. The absorption of N-nitrosomethylaniline and N-nitrosodiphenylamine and their ortho-, meta-, and para-nitro derivatives in seven different solvents in the region of  $2200-7000 \text{ \AA}$  was measured.

2. According to data on the absorption curves, the replacement of the hydrogen on the nitrogen of a secondary aromatic amine by a nitroso group does not affect the electron-donor character of the amino group.

3. In dilute acids and in the presence of sodium alcoholate, with nitro-N-nitrosodiphenylamines, as with some nitro-N-nitrosomethylanilines in dilute sulfuric acid, there is elimination of the effect of the nitroso group on the absorption.

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## S-DERIVATIVES OF THIOUREA

### III. REACTIONS OF THIOUREA WITH N-(2,3-DIBROMOPROPYL)-PHTHALIMIDE

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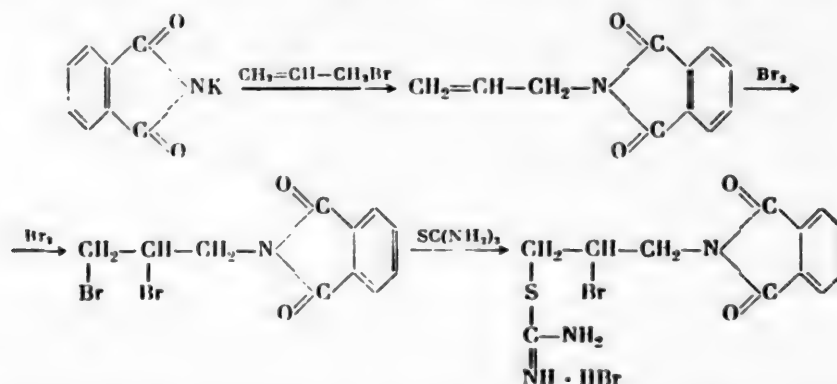
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November, 1960

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It was shown previously [1] that the reaction of thiourea with N,N-dialkyl-2,3-dibromopropylamines forms the corresponding diisothiuronium derivatives. The reaction of thiourea with 2,3-dibromopropylamine and its N-monoalkyl derivatives leads to the corresponding 2-imino-3-alkyl-5-isothiuroniummethylthiazolidines. At the same time, it was shown that the reaction of thiourea with N-acetyl-2,3-dibromopropylamine leads not to a thiazolidine ring, but a diisothiuronium derivative. Thus, a reduction in the basicity of the amine changes its behavior under the conditions of the reaction studied.

It therefore seemed interesting to study the reaction of thiourea with N-(2,3-dibromopropyl)-phthalimide, where the nitrogen does not have basic properties. The reaction was carried out in solvents with various boiling points and polarities. A single reaction product was obtained in all cases as was demonstrated by paper chromatography. The reaction product was isolated from the reaction mixture with the reaction carried out in isobutanol. Analysis data showed that the reaction yielded a mono- and not a diisothiuronium derivative. Thus, the presence of the phthalyl protective group on the amino group sharply reduced the reactivity of one of the bromine atoms. It is logical to assume that the phthalyl group affected the secondary bromine atom lying closest to it and the replacement of the primary bromine atom occurred quite readily during the reaction with thiourea. The reaction product therefore was probably N-[2-bromo-3-(isothiuronium bromide)propyl]-phthalimide.



Increasing the reaction time to 24 hr and also using a 16-fold excess of thiourea did not yield even traces of a diisothiuronium derivative. The second bromine atom was not replaced either when the pure monoisothiuronium derivative was treated with excess thiourea.

For determining the rate of reaction of thiourea with N-(2,3-dibromopropyl)-phthalimide, thiourea containing the radioactive isotope of sulfur  $\text{S}^{35}$  was used in the reaction and this made it possible to carry out radio-

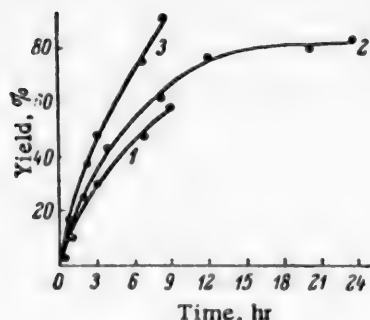


Fig. 1. Relation of N-[2-bromo-3-(isothiuronium bromide)-propyl]-phthalimide yield to the time of reaction in isobutanol. 1) Equimolecular concentrations of reagents; 2) 2-fold excess of thiourea; 3) 2-fold excess of dibromopropyl-phthalimide.

chromatographic analysis. When a twofold excess of thiourea was used the reaction was practically complete in 12 hr; the yield of the mono-isothiuronium derivative was 80% (Fig. 1).

If the starting materials were in equimolecular concentrations, the yield of the reaction product reached 63% after 8 hr; the use of a twofold excess of the dibromide increased the yield to 90% after the same time (Fig. 1).

As a result of these investigations it was possible to find a convenient preparative method for obtaining N-[2-bromo-3-(isothiuronium bromide)-propyl]-phthalimide.

## EXPERIMENTAL

N-Allylphthalimide. This compound was prepared from potassium phthalimide and allyl bromide [2] in 67% yield. The m. p. was 69° (from ethanol).

N-2,3-Dibromopropylphthalimide. This compound was prepared by bromination of N-allylphthalimide in chloroform [3]. After removal of the solvent, the residue was washed with ether and recrystallized. The yield was 78% and the m. p. 109-110° (from isobutanol).

### Reaction of Thiourea with N-(2,3-dibromopropyl)-phthalimide

A solution of 0.722 g of dibromopropylphthalimide and 0.316 g of thiourea in 5 ml of dry isobutanol was boiled for 12 hr. The course of the reaction was followed by paper chromatography (ascending method). The mobile solvent was the organic layer of a mixture of butanol, acetic acid, and water (4:1:5). Grote's reagent [4] was used to give a color reaction. The reaction was carried out analogously in ethanol, isopropanol, acetone, acetic acid, and dimethylformamide. The reaction was carried out at 60° in dimethylformamide. The solvent was removed in vacuum, the unreacted dibromide extracted with chloroform, and the residual oil crystallized by trituration in absolute ether. It was not possible to free the reaction product from thiourea by recrystallization and therefore the mixture was separated on a column of paper pulp. This was possible due to the large difference in the  $R_f$  values of thiourea (0.51) and the reaction product (0.80). The height of the column was 54 cm, the diameter 15 mm, and the eluting solvent aqueous butanol. The elution was followed by paper chromatography and measurement of the refractive index of the eluate. After removal of the butanol in vacuum, from 200 mg of mixture we obtained 70 mg of chromatographically pure product with  $R_f$  0.80 and m. p. 195°.

The separation of 500 mg of the mixture on the same column was not complete and therefore the reaction product was converted to the picrate for further purification. For this purpose, an aqueous solution of the mixture of the reaction product and thiourea was poured into a saturated aqueous solution of picric acid. The product gave an insoluble picrate, while the thiourea remained in solution. The precipitate was collected and the isothiuronium picrate converted into the hydrobromide by passing a methanol solution of the picrate through a column of AN-2F ion-exchange resin in the hydrobromide form. The height of the column was 37 cm, the diameter 15 mm, and the elution rate 10 drops/min. The white crystalline substance obtained after removal of the methanol in vacuum was chromatographically pure ( $R_f$  = 0.80) and had m. p. 196°.

Found %: C 34.33, 34.16; H 2.86, 2.72; N 9.33, 9.54; Br 18.79, 18.95.  $C_{12}H_{15}O_2N_3SBr$ . Calculated %: C 34.14, H 3.10; N 9.95; Br 18.89.

The picrate had m. p. 202.5-204° (from methanol).

Found %: C 38.18, 38.33; H 2.78, 2.92; N 14.43, 14.31.  $C_{16}H_{15}O_9N_5SBr$ . Calculated %: C 37.84; H 2.64; N 14.70.

### Radiochromatographic Analysis

Study of reaction rate. a) With a twofold excess of thiourea. A solution of 0.644 g of dibromopropyl-phthalimide and 0.283 g of thiourea with a specific activity of  $5.2 \cdot 10^3$  counts/min · g in 25 ml of dry isobutanol was boiled for 24 hr. At definite times, samples of the reaction mixture were removed with a special



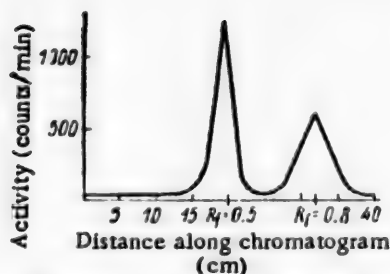


Fig. 2. Distribution of activity between thiourea ( $R_f$  0.50) and N-[2-bromo-3-(isothiuronium bromide)-propyl]-phthalimide ( $R_f$  0.80) in the reaction in isobutanol after 24 hr (ratio of dibromopropylphthalimide to thiourea of 1:2).

capillary, 0.005 ml in volume, and deposited on strips of chromatography paper (type "M" of the Volodarskii Leningrad Factory), 4 cm wide. The chromatograms were run under identical conditions, dried in air, and cut parallel to the solvent front into strips 4 × 0.5 cm. The count rate of each strip was measured under standard conditions on an end-window counter. Figure 2 gives the distribution of activity along a chromatogram of a sample taken after completion of the reaction. The total activity of the spot, which was proportional to the amount of substance in the spot, was calculated by summing the activity of strips whose count rate exceeded the background.

b) With equimolecular concentrations of reagents. A solution of 0.202 g of dibromopropylphthalimide and 0.049 g of thiourea in 6 ml of anhydrous isobutanol was boiled for 8 hr. Data from radiochromatographic analysis are given in Fig. 1 (curve 1).

c) With a twofold excess of N-(2,3-dibromopropyl)-phthalimide. A solution of 0.268 g of dibromopropylphthalimide and 0.028 g of thiourea in 5 ml of anhydrous isobutanol was boiled for 8 hr. Data from radiochromatographic analysis are given in Fig. 1 (curve 3).

Preparation of N-[2-bromo-3-(isothiuronium bromide)-propyl]-phthalimide. A solution of 7.29 g of dibromopropylphthalimide and 1.32 g of thiourea in 30 ml of anhydrous isobutanol was boiled for 10 hr. The precipitate was collected and recrystallized. The yield was 4.91 g (67%) and the m. p. 196° (from ethanol).

#### SUMMARY

It was established that only one bromine atom is replaced in the reaction of N-(2,3-dibromopropyl)-phthalimide with thiourea. It is considered that the reaction product is N-[2-bromo-3-(isothiuronium bromide)-propyl]-phthalimide and a preparative method is proposed for obtaining the latter.

Some kinetic characteristics of the reaction studied were determined by paper radiochromatography.

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SYNTHESIS OF ESTERS AND OTHER DERIVATIVES  
OF CARBOXYLIC ACIDS BY ACID CATALYSIS  
FROM CARBON MONOXIDE, OLEFINS, AND  
ACYLATING COMPOUNDS

IV. CARBOMETHOXYLATION OF AMYLENES OF VARIOUS STRUCTURES

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We previously reported the catalytic synthesis of carboxylic esters from olefins, carbon monoxide, and alcohols in the presence of concentrated sulfuric acid [1]. The behavior of butylene and isobutylene [2], 1-hexene and 1-pentene [3], and cyclopentene and cyclohexene [4] in this reaction has been investigated. It was shown that normal  $\alpha$ -olefins generally give as the main reaction product an ester of the alkanoic acid with one more carbon atom than the starting olefin and two methyl groups in the  $\alpha$ -position. An ester of the isomeric acid with one ethyl group in the  $\alpha$ -position is obtained in lower, but still considerable yield. This is particularly true in the case of the carbalkoxylation of pentenes contained in the  $C_5$ - $C_8$  fraction of synthol, which are converted into  $\alpha,\alpha$ -dimethylbutyric and  $\alpha$ -ethylbutyric esters [3].

In the present work we give the experimental results obtained during carbomethoxylation of the following isomeric amylenes by the same method: 1-pentene, 3-methyl-1-butene, 2-methyl-1-butene, and 2-methyl-2-butene. As in previous work [1-4], the reaction of the olefin, carbon monoxide, and catalyst, concentrated sulfuric acid, proceeded in the first stage of the process at an initial pressure of 80 atm of CO and 20-40° with the formation of acylsulfuric acids as intermediate products. In the second stage, the latter were converted to methyl esters by the addition of methanol to the reaction mixture. The yield of methyl esters obtained from 1-pentene was 54%, while that from branched amylenes was 64-69% of the starting olefin. The highest yield (69%) was obtained with 2-methyl-2-butene. The main reaction product from all the isomeric amylenes was methyl  $\alpha,\alpha$ -dimethylbutyrate, whose content in the mixture of esters obtained was 50.5% by volume in the experiment with 1-pentene, 61% with 3-methyl-1-butene, 45% with 2-methyl-1-butene, and 35% with 2-methyl-2-butene. The nature of the remaining reaction products, however, varied, depending on whether the starting amylene had a normal or iso structure. In complete analogy with the results obtained with 1-hexene and 1-heptene, in the case of 1-pentene the second reaction product was methyl  $\alpha$ -ethylbutyrate, the content of which in the mixture of esters obtained from this olefin was 27.5%. This ester was not found in the reaction products of the branched olefins, which were partly converted into methyl esters of trimethylacetic (4-10%),  $\alpha,\alpha$ -dimethylvaleric (0-5%), and higher-molecular acids (30-50%).

In the two-stage synthesis of carboxylic acid from olefins, carbon monoxide, and water in the presence of sulfuric acid, Koch obtained  $\alpha$ -methylvaleric acid from 1-pentene in addition to  $\alpha,\alpha$ -dimethylbutyric and  $\alpha$ -ethylbutyric acids, while he obtained only  $\alpha,\alpha$ -dimethylbutyric acid from 2-methyl-1-butene [5]. On replacing carbon monoxide by formic acid and carrying out the reaction at atmospheric pressure, Koch and Haaf [6] obtained a mixture of  $\alpha,\alpha$ -dimethylbutyric,  $\alpha$ -methylvaleric,  $\alpha$ -ethylbutyric, and higher ( $C_{11}$ ) acids from

**TABLE 1**  
Carbomethoxylation of Amylenes

Reagents (ml)			CO pressure (atm)		CO absorbed		Yield of esters	
sulfuric acid	amylenes	methanol	initial	final	liter	% of theoretical	ml	% of starting amylenes
250	1-Pentene (150)	150	80	52	22.4	73.2	112	54.3
500	3-Methyl-1-butene (150)	250	80	48	19.8	60.0	135	63.5
500	2-Methyl-1-butene (200)	250	80	35	26.0	61.2	190	67.0
500	2-Methyl-2-butene (100)	150	80	60	11.8	56.0	98	69.0

**TABLE 2**  
Esters Obtained from Amylenes, Carbon Monoxide, and Methanol

Starting amylenes	Methyl ester of the acid	Content of ester (vol. % of ester mixture obtained)	Boiling point	$d_4^{20}$	$n_D^{20}$	Melting point of anilide
1-Pentene	$\alpha, \alpha$ -Dimethylbutyric	50.7	127—127.5°	0.8820	1.4022	92°
	$\alpha$ -Ethylbutyric	27.5	136—137.4	0.8790	1.4018	125
3-Methyl-1-butene	Trimethylacetic	4.0	101.5—102.5	0.8685	1.3892	133
	$\alpha, \alpha$ -Dimethylbutyric	61.0	127.2—127.4	0.8812	1.4022	92
2-Methyl-1-butene	Trimethylacetic	10.0	101.5—101.8	0.8733	1.3898	133
	$\alpha, \alpha$ -Dimethylbutyric	45.2	127.4—127.6	0.8819	1.4024	92
2-Methyl-2-butene	$\alpha, \alpha$ -Dimethylvaleric	5.1	150.3—150.8	0.8756	1.4072	71
	Trimethylacetic	5.0	101.2—101.6	0.8730	1.3895	133
	$\alpha, \alpha$ -Dimethylbutyric	35.0	127.1—127.3	0.8821	1.4022	92
	$\alpha, \alpha$ -Dimethylvaleric	3.0	146.8—148.0	0.8856	1.4115	71

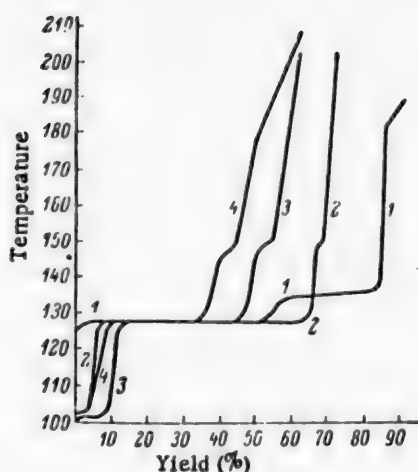
2-pentene and a mixture of trimethylacetic,  $\alpha, \alpha$ -dimethylbutyric,  $\alpha, \alpha$ -dimethylvaleric, and higher acids from 2-methyl-2-butene.

#### EXPERIMENTAL

In the work we used pure preparations of amylenes, whose syntheses were described previously [7, 8]. They had the following constants:

1-pentene — b. p. 29.0° (760 mm),  $n_D^{20}$  1.3717,  $d_4^{20}$  0.6403; 3-methyl-1-butene — b. p. 20.0° (760 mm),  $n_D^{20}$  1.3641;  $d_4^{20}$  0.6270; 2-methyl-1-butene — b. p. 31.0° (760 mm),  $n_D^{20}$  1.3778,  $d_4^{20}$  0.6502; 2-methyl-2-butene — b. p. 38.6° (760 mm),  $n_D^{20}$  1.3874,  $d_4^{20}$  0.6622.

The procedure for the synthesis of esters from olefins, carbon monoxide, and alcohols under pressure was described previously [2]. The first stage was carried out in a stainless steel autoclave with a turbine stirrer operating at 800 rev/min and a drop injector for adding liquid olefin. The autoclave was charged with 0.25–0.5 liter of concentrated sulfuric acid ( $d$  1.84), 80 atm of carbon monoxide introduced, and the starting amylenes added over a period of 1 hr from the drop injector. When the absorption of carbon monoxide had ceased, the reaction mixture was removed from the autoclave and 150–250 ml of methanol and 1.5 liter of water were added. The methyl esters of the carboxylic acids liberated were washed with 10% sodium carbonate solution and water, dried over anhydrous copper sulfate, and distilled on a column with an efficiency of 90 theoretical plates. From



Distillation curves of methyl esters obtained from 1-pentene (1), 3-methyl-1-butene (2), 2-methyl-1-butene (3), and 2-methyl-2-butene (4).

fractions corresponding to individual esters, we prepared anilides of the acids, which were used to identify these esters (mixed melting points with known anilides).

The conditions of separate experiments on carbomethoxylation of amylenes and the results obtained are given in Tables 1 and 2. The distillation curves of the mixtures of esters obtained are given in the figure. The data presented show that mixtures of methyl esters of the following acids were obtained: from 1-pentene -  $\alpha, \alpha$ -dimethylbutyric and  $\alpha$ -ethylbutyric (in a volume ratio of ~2:1); from 3-methyl-1-butene -  $\alpha, \alpha$ -dimethylbutyric and trimethylacetic (in ratio of 15:1); from 2-methyl-1-butene -  $\alpha, \alpha$ -dimethylvaleric (in a ratio of 11:1:1.2), and from 2-methyl-2-butene - esters of the same acids (in a ratio of 12:1.6:1) and high-molecular acids (more than 50%).

According to literature data, methyl  $\alpha, \alpha$ -dimethylbutyrate has: b. p. 125-125.5° (746 mm),  $d_4^{25}$  0.8943,  $n_D^{25}$  1.3991 [9]; the anilide of this acid has m. p. 91-92° [10]; methyl  $\alpha$ -ethylbutyrate: b. p. 135-137° (736 mm),  $d_4^{25}$  0.8886,  $n_D^{25}$  1.40669 [11]; the anilide has m. p. 124.3-124.5° [12]; methyl trimethylacetate: b. p. 100-102°,  $d_4^{20}$  0.891 [13]; the anilide has m. p. 132-133° [14]; methyl  $\alpha, \alpha$ -dimethylvalerate: b. p. 144-145° [15]; the anilide has m. p. 70.5-74° [16].

#### SUMMARY

1. Methyl esters of carboxylic acids were obtained in yields of 55-70% on the starting olefin from amylenes of various structures, carbon monoxide, and methanol at 20-40° and a CO pressure of 80 atm in the presence of sulfuric acid.

2. The main reaction product was methyl  $\alpha, \alpha$ -dimethylbutyrate (35-61%). We also obtained smaller amounts of methyl  $\alpha$ -ethylbutyrate (27.5%) from 1-pentene and methyl trimethylacetate (4-10%) from branched amylenes. Methyl  $\alpha, \alpha$ -dimethylvalerate (3-5%) was also obtained from 2-methyl-1-butene and 2-methyl-2-butene.

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# SYNTHESIS OF SOME FUNCTIONAL DERIVATIVES OF 2,5-DIPHENYL-1,3,4-OXADIAZOLE

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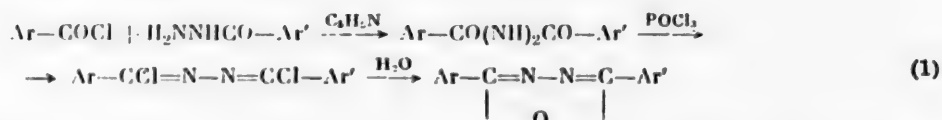
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November, 1960

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As a development of previous work [1-4] on the preparation of scintillating materials consisting of 1,3,4-oxadiazole derivatives, among which extremely efficient scintillators have been found [4-7], the syntheses of new functional derivatives of this class are described in the present communication.

By the scheme described previously [2, 8]

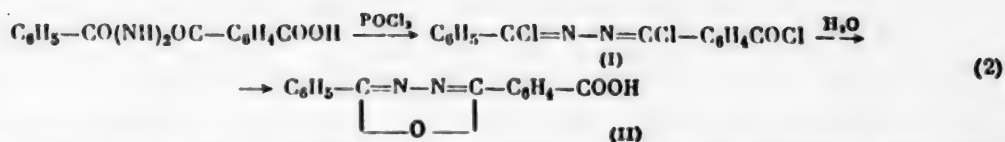


we prepared para derivatives of 2,5-diphenyl-1,3,4-oxadiazole with the following substituents: F, SCH<sub>3</sub>, CH<sub>3</sub>, iso-OC<sub>3</sub>H<sub>7</sub>, N(CH<sub>3</sub>)<sub>2</sub>, COOH, COOC<sub>2</sub>H<sub>5</sub>. The synthesis scheme presented was extended to all the isomeric mono-functional derivatives of 2,5-diphenyl-1,3,4-oxadiazole. In this way, the first representatives of ortho and meta derivatives of oxadiazole with nitro, chloro, methoxy, and methyl groupings were prepared. During the synthesis it was found that the reaction conditions and also the yields did not differ substantially from those for the para derivatives, regardless of the position and form of the substituent. As a result, it was possible to develop a general method for preparing functional derivatives of oxadiazole and the diarylhydrazines from which they were obtained.

It should be noted that contrary to literature data [8], diarylhydrazines are formed even in the cold. Reactions at high temperatures gave appreciable amounts of by-products, namely, symmetrical diarylhydrazines of the type (C<sub>6</sub>H<sub>5</sub> - CONH)<sub>2</sub> and (X - C<sub>6</sub>H<sub>4</sub> - CONH)<sub>2</sub>, and this was observed particularly when the phenyl ring contained electron-acceptor substituents (NO<sub>2</sub> and COOC<sub>2</sub>H<sub>5</sub>). In the preparation of the oxadiazole, the time that the diarylhydrazine was heated with phosphorus oxychloride could be limited to that required for complete solution of the former instead of boiling for many hours as recommended in the literature [8, 9].

The use of scheme (1) may be complicated by the reaction of the functional groups with the reagents used. In these cases, some substituents were converted into others in the oxadiazole molecule (reduction of nitro compounds to amines with phenylhydrazine, Sandmeyer reaction, and hydrolysis of a nitrile to an amide [10]), and this showed that these reactions were applicable in the oxadiazole series. However, hydrolysis of the ester group in 2-(p-carbomethoxyphenyl)-5-phenyl-1,3,4-oxadiazole to prepare the acid was accompanied by rupture of the oxadiazole ring with the result that 1-(p-carboxybenzoyl)-2-benzoylhydrazine was isolated. The latter was treated with phosphorus oxychloride according to scheme (2) to give the acid chloride (I), which was cyclized in water with the simultaneous hydrolysis of the acid chloride group to yield 2-(p-carboxyphenyl)-5-phenyl-1,3,4-oxadiazole (II).





All the oxadiazoles and diaroylhydrazines synthesized were colorless crystalline substances, which were soluble in dioxane and alcohol, less soluble in benzene, and insoluble in water. Their solubility in organic solvents increased from para to ortho isomers, while the melting points correspondingly decreased.

#### EXPERIMENTAL\*

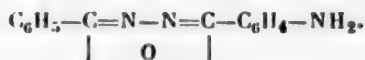
General procedure for preparing diaroylhydrazines of the type  $\text{C}_6\text{H}_5-\text{CO}(\text{NH})_2\text{OC}-\text{C}_6\text{H}_4-\text{X}$ . To a solution of 0.1 mole of the hydrazide of the aromatic acid in dry pyridine (0.8 mole) was added 0.1 mole of the aromatic acid chloride in small portions with vigorous stirring. The reaction was exothermic. It is recommended that the temperature is kept below 60°. When all the acid chloride had been added, the reaction mixture was left to cool and then poured into 500 ml of cold water with stirring. When the hydrazide was sparingly soluble in pyridine, the order of addition of the reagents could be changed so that the hydrazide was added to a pyridine solution of the acid chloride under analogous conditions. After the mixture had stood for half an hour, the precipitated diaroyl hydrazine was collected, washed with water until the odor of pyridine disappeared and then alcohol, and dried. The product obtained was recrystallized to constant melting point from dioxane, ethanol, or glacial acetic acid.

The diaroylhydrazines synthesized by this method and their characteristics are given in Table 1.

General procedure for preparing oxadiazoles of the type  $\text{C}_6\text{H}_5-\text{C}=\text{N}-\text{N}=\text{C}-\text{C}_6\text{H}_4-\text{X}$ . A mixture of 0.1

mole of the diaroylhydrazine and 1 mole of phosphorus oxychloride was heated and stirred in a round-bottomed flask, fitted with a reflux condenser and stirrer, until the diaroylhydrazine dissolved completely and then heating was continued for a further 15 min. The mass darkened. The reaction mixture was then cooled (silky crystals sometimes separated) and gradually added to 600 ml of cold water with stirring. The mixture evolved heat and the temperature was not allowed to rise above 50-60°. When the mixture had cooled, the oxadiazole was collected, washed with water and alcohol, and dried. It was purified by recrystallization from dioxane or alcohol and by passage through a semicontinuous chromatography column [11] packed with alumina gel with benzene or toluene as the solvent. The oxadiazoles obtained by the method presented and their characteristics are given in Table 2.

General procedure for preparing aminoderivatives of 2,5-diphenyl-1,3,4-oxadiazole.



A mixture of 0.02 mole of 2-(nitrophenyl)-5-phenyl-1,3,4-oxadiazole and 0.12 mole of phenylhydrazine was heated and stirred until the nitro compound dissolved completely. The evolution of nitrogen began at 80-90° and the mass darkened. The temperature was carefully (to avoid an explosion) raised to 110-120°. When the reaction moderated and the solution began to lighten, the temperature was raised to 150-160° and kept at this level until the solution became light yellow and the evolution of bubbles almost ceased. The solution was then cooled to 120°, poured with stirring into 200 ml of benzene, and left for about 1 hr. The colorless or yellowish precipitate was collected, washed on the filter with benzene and diethyl ether, and dried in vacuum at room temperature. The amines synthesized, whose characteristics are given in Table 2, were colorless crystalline substances, which were soluble in dioxane, less so in alcohol and benzene, and almost insoluble in water.

Synthesis of 2-(p-dimethylaminophenyl)-5-phenyl-1,3,4-oxadiazole. A mixture of 14 g of 1-(p-dimethylaminobenzoyl)-2-benzoylhydrazine and 40 ml of phosphorus trioxide was heated until solution was complete. After cooling, the mixture was poured into 1.5 liter of cold water. The reaction mixture was neutralized with ammonia to decompose the hydrochloride. The precipitate was collected, washed with water and ethanol, and dried. The yield was 12.9 g (99%) and the m. p. 141-142°. After chromatographic purification on alumina gel

\*L. N. Kulakova and L. M. Egupova helped with the experimental work.



TABLE 1

Diaroylhydrazines Synthesized  $C_6H_5-CO(NH)_2OC-C_6H_4-X$ 

Sample No.	o-Benzoylhydrazine	Yield %	Melting point	Empirical formula	% N	
					found	calc.
1	1-(p-Dimethylaminobenzoyl)-	92	236°	$C_{16}H_{17}O_2N_3$	14.93	14.85
2	1-(p-Carboethoxybenzoyl)-	83	152	$C_{17}H_{16}O_4N_2$	9.03	8.97
3	1-(p-Carboxybenzoyl)-	94	282	$C_{15}H_{12}O_4N_2$	9.69	9.86
4	1-(p-Fluorobenzoyl)-	99	210	$C_{14}H_{11}O_2N_2F$	11.08	10.85
5	1-(p-Methylbenzoyl)-	66	220	$C_{15}H_{14}O_2N_2$	11.20	11.02
6	1-(p-Methylmercaptobenzoyl)-	76	185	$C_{15}H_{14}O_2N_2S$	10.01	9.81
7	1-(p-Isopropoxybenzoyl)-	80	202	$C_{17}H_{18}O_3N_2$	9.23	9.38
8	1-(m-Nitrobenzoyl)-	60	216	$C_{14}H_{11}O_4N_3$	14.50	14.73
9	1-(m-Methylbenzoyl)-	98	210	$C_{15}H_{14}O_2N_2$	11.28	11.02
10	1-(m-Methoxybenzoyl)-	77	213	$C_{15}H_{14}O_3N_2$	10.61	10.37
11	1-(o-Chlorobenzoyl)-	87	179	$C_{14}H_{11}O_2N_2Cl$	10.02	10.21
12	1-(o-Nitrobenzoyl)-	67	214	$C_{14}H_{11}O_4N_3$	14.80	14.73
13	1-(o-Methoxybenzoyl)-	73	145	$C_{15}H_{14}O_3N_2$	10.67	10.37

Note: Compounds 1 and 8 were recrystallized from glacial acetic acid with activated charcoal, 2-7, 9, and 10 from ethanol with activated charcoal, and 11-13 from ethanol and toluene. Compound 5 was also obtained by another method [13].

TABLE 2

Oxadiazoles Synthesized  $C_6H_5-C=N-N=C-C_6H_4-X$ 

Sample No.	5-Phenyl-1,3,4-oxadiazole	Yield %	Melting point	Empirical formula	% N	
					found	calc.
1	2-(p-Dimethylaminophenyl)-	98	143°	$C_{16}H_{15}ON_3$	16.05	15.84
2	2-(p-Carboethoxyphenyl)-	99	140	$C_{17}H_{14}O_3N_2$	9.57	9.52
3	2-(p-Carboxyphenyl)-	97	220-230	$C_{15}H_{10}O_3N_2$	10.21	10.53
			Sublimed			
4	2-(p-Fluorophenyl)-	59	147	$C_{14}H_9ON_2F$	11.93	11.66
5	2-(p-Tolyl)-	65	117	$C_{15}H_{12}ON_2$	11.95	11.86
6	2-(p-Methylmercaptophenyl)-	82	185	$C_{15}H_{12}ON_2S$	10.64	10.44
7	2-(p-Isopropoxyphenyl)-	70	80	$C_{17}H_{16}O_3N_2$	10.29	10.00
8	2-(p-Cyanophenyl)-	91	183	$C_{15}H_8ON_3$	17.26	17.00
9	2-(p-Amidophenyl)-	75	221 (dec.)	$C_{15}H_{11}O_2N_3$	15.98	15.84
10	2-(m-Nitrophenyl)-	99	147	$C_{14}H_9O_3N_3$	15.88	15.73
11	2-(m-Tolyl)-	99	96	$C_{15}H_{12}ON_2$	11.62	11.86
12	2-(m-Methoxyphenyl)-	97	72	$C_{15}H_{12}O_3N_2$	11.42	11.11
13	2-(m-Aminophenyl)-	68	162	$C_{14}H_{11}ON_3$	17.76	17.72
14	2-(o-Chlorophenyl)-	90	105	$C_{14}H_9ON_2Cl$	10.85	10.92
15	2-(o-Nitrophenyl)-	86	121	$C_{14}H_9O_3N_3$	15.97	15.73
16	2-(o-Methoxyphenyl)-	99	94	$C_{15}H_{12}O_3N_2$	10.69	11.11
17	2-(o-Aminophenyl)-	76	176	$C_{14}H_{11}ON_3$	17.49	17.72

Note: Compounds 1, 4, 5, 7, and 11-13 were recrystallized from ethanol, 2 from dioxane and toluene and 6, 10, and 14-17 from benzene. Compound 5 was also obtained by another method [13].

with toluene as the solvent, the substance formed colorless crystals with m. p. 142-143°, which were moderately soluble in alcohol and benzene and insoluble in water.

Found %: N 16.05,  $C_{16}H_{15}ON_3$ . Calculated %: N 15.84.

Synthesis of 2-(p-cyanophenyl)-5-phenyl-1,3,4-oxadiazole. A 1.9 g sample of well-purified 2-(p-amino-phenyl)-5-phenyl-1,3,4-oxadiazole (with m. p. not less than 187°) was dissolved in 50 ml of hot 18% hydrochloric acid and the suspension which formed on cooling was diazotized with sodium nitrite solution. The unreacted precipitate remaining after diazotization was removed by filtration and the filtrate adjusted to pH 5-6 with sodium carbonate and then gradually added with cooling and stirring to a solution of  $\text{KCu}(\text{CN})_2$  [12]. The reaction mixture foamed and deposited a brown precipitate. After the mixture had been kept for 12 hr, the precipitate was collected, washed with water and alcohol, and dried. The yield was 1.8 g (91%) and the m. p. 168°. The product was then dissolved in a mixture of dioxane and alcohol (1:2) and precipitated with water. It was again dissolved in the same mixture, but with treatment with activated charcoal, the filtrate evaporated in vacuum, and the precipitated crystals collected, washed with alcohol, and dried. The m. p. was 183°.

Synthesis of 2-(p-amidophenyl)-5-phenyl-1,3,4-oxadiazole. To a solution of 0.1 g of 2-(p-cyanophenyl)-5-phenyl-1,3,4-oxadiazole in ethanol was added 1.5 ml of 2 N aqueous potassium hydroxide and then 0.2 ml of 30% hydrogen peroxide. After 15 min heating, which was accompanied by oxygen evolution, the solution was neutralized with acid. The precipitate was collected, washed with alcohol, and dried. The yield was 0.9 g (75%) and the m. p. 221° (decomp.).

2-(p-Cyanophenyl)-5-phenyl-1,3,4-oxadiazole formed colorless crystals, which were soluble in dioxane, less so in alcohol, benzene, and acetone, and insoluble in water.

Found %: N 17.26.  $\text{C}_{15}\text{H}_9\text{ON}_3$ . Calculated %: N 17.00.

2-(p-Amidophenyl)-5-phenyl-1,3,4-oxadiazole formed colorless crystals, which were sparingly soluble in alcohol and insoluble in water.

Found %: N 15.98.  $\text{C}_{15}\text{H}_{11}\text{O}_2\text{N}_3$ . Calculated %: N 15.84.

Hydrolysis of 2-(p-carbethoxyphenyl)-5-phenyl-1,3,4-oxadiazole. A 1.1 g sample of 2-(p-carbethoxyphenyl)-5-phenyl-1,3,4-oxadiazole was boiled with 30 ml of 2% aqueous sodium hydroxide solution until the substance dissolved (about 3 hr). The solution was neutralized with hydrochloric acid and the flocculent precipitate of 1-(p-carboxybenzoyl)-2-benzoylhydrazine collected, washed with water, and dried. The yield was 1 g (94%). After recrystallization from pyridine, the substance appeared as colorless crystals with m. p. 280-285° (sublimed).

Found %: N 9.69.  $\text{C}_{15}\text{H}_{11}\text{O}_4\text{N}_2$ . Calculated %: N 9.86.

#### SUMMARY

1. General procedures were developed for the synthesis of all isomeric monofunctional derivatives of 2,5-diphenyl-1,3,4-oxadiazole and the diarylhydrazines from which they were obtained.
2. The chemical conversions of some functional derivatives of 2,5-diphenyl-1,3,4-oxadiazole substituted in the phenyl ring were studied.
3. Seventeen oxadiazoles that have not been described in the literature and thirteen diarylhydrazines were synthesized and their properties studied.

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## REACTIONS OF AROMATIC NITRO COMPOUNDS

### IX. SPATIAL HINDRANCE IN NUCLEOPHILIC SUBSTITUTION

S. S. Gitis and A. I. Glaz

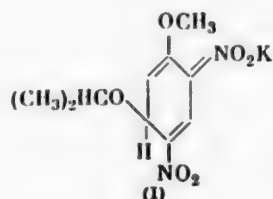
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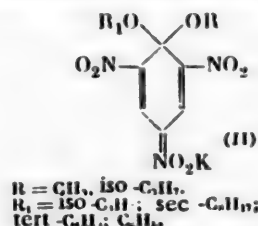
The reaction of transesterification of alkyl and aryl ethers of 2,4-di- and 2,4,6-trinitrophenols belongs to the reactions of nucleophilic substitution which occur by a bimolecular  $S_N2$  mechanism. The replacement of one alkoxy group by another occurs through the step of formation of an intermediate addition product of the corresponding alcoholate, which for ethers of trinitrophenol is easily isolated as a colored salt; in the case of dinitrophenol the intermediate reaction product has not been isolated [1-3].

In one of our reports [3] we could not replace the methoxy group in 2,4-dinitroanisole by the isopropoxy group. We explained this by the spatial effect of the nitro groups in the ortho group to the carbon atom combined with a methoxy group. We ascribed the occurrence of an intense color to the formation of a product with structure (I).



However, in later work [4] on the model molecules 3-methoxy-4,6-dinitrotoluene and 1,3-dimethoxy-4,6-dinitrobenzene it was shown that formation of an intermediate product with the above structure did not occur. This forced us once more to repeat the study of the reaction of potassium isopropylate with 2,4-di- and 2,4,6-trinitroanisole. The results of the study showed that di- and trinitroanisoles form intermediate colored products in benzene not only with the isopropylate, but also with potassium sec-n-octylate, tert-butylate and phenolate. Moreover, the isopropyl ethers of 2,4-di- and 2,4,6-trinitrophenols also formed colored addition products with the above alcoholates.

Thus, not only the methoxy group, but even the isopropoxy group does hinder the addition of alkoxy groups with strongly branched radicals on the carbon atom of the benzene ring on which they occur (II).



However, as can easily be seen from the models, two alkoxy groups project from the plane of the ring and so for the formation of addition products require a great expenditure of energy, which is strongly reflected in the yields of the resulting products. Thus, for example, with an equimolecular ratio of reacting components, the yield of addition product of potassium *tert*-butylate to trinitroanisole is 15% while the yield of addition product of potassium *n*-butylate to trinitroanisole is 89% [2]. The yield of colored product can be increased only by shifting the equilibrium of the reaction by addition of a great excess of alcoholate. In this case the yield of addition product of, for example, potassium *tert*-butylate to the isopropyl ether of 2,4,6-trinitrophenol can be brought to 95%. It should be noted that the presence in the intermediate products of alkoxy groups with radicals of similar structures increases the stability of the molecule. All the addition products of potassium alcoholates to trinitroanisole have corresponding decomposition temperatures lower than the addition products of these alcoholates to the isopropyl ether of trinitrophenol.

The second stage in the transesterification process is the decomposition of the intermediate with water, as we showed previously [5]; it is characterized by the splitting off of the one alkoxy group which has the greatest negative induction effect. There is also always partial formation of potassium trinitro- or dinitrophenolates. The noncoplanarity of the system, however, also affects this step of the reaction so that one alkoxy group is not always replaced by another. The addition product of potassium isopropylate to trinitroanisole gives, after decomposition by water, up to 15% of the isopropyl ether of trinitrophenol; the addition product of potassium *tert*-butylate to trinitroanisole after decomposition gives 10% of the starting trinitroanisole. Thus, the *tert*-butyl ether of trinitrophenol could not be isolated. After decomposition by water of the addition product of potassium *sec*-*n*-octylate to trinitroanisole or the isopropyl ether of trinitrophenol we obtained only potassium picrate. Such a transformation can probably be explained by assuming that in the decomposition by water there is conversion of a noncoplanar system to a coplanar one, related to the considerable spatial effect of the nitro groups in the ortho-position between which can be placed no sort of branched alkoxy groups. Therefore, under the influence of an attacking hydroxyl ion, both alkoxy groups are split out, with formation of picrates.

The decomposition of the intermediate addition products of potassium isopropylate to dinitroanisole gives a 75% yield of the isopropyl ether of 2,4-dinitrophenol. The addition products of potassium *tert*-butylate and *sec*-*N*-octylate to dinitroanisole after decomposition by water give quantitatively the unchanged dinitroanisole.

It is interesting to note that in the decomposition by water of the addition products of potassium isopropylate and *tert*-butylate to the isopropyl ether of trinitrophenol the yield of isopropyl ether more than doubles compared to the yield of this ether from the addition product of potassium isopropylate to trinitroanisole, and the amount of picrate decreases. This fact can be explained by the decreased positive charge of the carbon atom on which occurs the isopropoxy group, more of an electron donor than methoxy. The decreased positive charge on the carbon atom makes somewhat difficult the addition of the hydroxyl ion.

The addition of potassium phenolate to trinitroanisole shows that, in spite of the weakening of the electron donor properties of the phenoxy group, the reaction of formation of an intermediate colored product occurs. Decomposition of this product by water, as would be expected, results in formation of trinitroanisole.

## EXPERIMENTAL

General method for obtaining addition products of potassium alcoholates to trinitroanisole. To a solution of 0.001 mole trinitroanisole in 20 ml of benzene was added a solution of 0.001 mole of KOH in the corresponding alcohol. The precipitate was separated and washed several times with ether. The product was easily soluble in water, less so in methanol, insoluble in benzene and ether.

Addition product of iso-C<sub>3</sub>H<sub>7</sub>OK. Red-orange powder with decomposition point 200°. Yield 51%.

Found %: K 11.58. C<sub>13</sub>H<sub>12</sub>O<sub>8</sub>N<sub>3</sub>K. Calculated %: K 11.44.

Addition product of *tert*-C<sub>4</sub>H<sub>9</sub>OK. Red needles with decomposition point 185°. Yield 15%.

Found %: K 10.78. C<sub>11</sub>H<sub>14</sub>O<sub>8</sub>N<sub>3</sub>K. Calculated %: K 10.98.

Addition product of *sec*-*n*-C<sub>8</sub>H<sub>17</sub>OK. Brown-red powder with decomposition point 160°. Yield 16%.

Found %: K 9.71. C<sub>15</sub>H<sub>23</sub>O<sub>8</sub>N<sub>3</sub>K. Calculated %: K 9.49.

Addition product of  $C_6H_5OK$ . To a solution of 0.0005 mole trinitroanisole in 10 ml of benzene was added a solution of 0.0005 mole of potassium phenolate in methanol. The precipitate was sucked off and washed several times with benzene to remove excess phenol, and then with ether. Bright red crystals with decomposition point  $205^\circ$ . Yield 65%.

Found %: K 10.78.  $C_{13}H_{10}O_8N_3K$ . Calculated %: K 10.40.

General method for obtaining addition products of potassium alcoholates to the isopropyl ether of picric acid. To a solution of 0.001 mole of the ether in 5 ml of benzene was added a concentrated solution of alcoholic alkali until precipitation stopped. The precipitate was sucked off and washed with a small amount of methanol, with benzene, and several times with ether.

Addition product of iso- $C_3H_7OK$ . Light brown powder with decomposition point  $210^\circ$ . Yield 65%.

Found %: K 10.72.  $C_{12}H_{16}O_8N_3K$ . Calculated %: K 10.57.

Addition product of tert- $C_4H_9OK$ . Intensely red crystals with decomposition point  $190^\circ$ . Yield 95%.

Found %: K 10.18.  $C_{13}H_{18}O_8N_3K$ . Calculated %: K 10.36.

Addition product of sec-n- $C_8H_{17}OK$ . Dark brown powder with decomposition point  $185^\circ$ . Yield 45%.

Found %: K 8.87.  $C_{16}H_{25}O_8N_3K$ . Calculated %: K 8.97.

Hydrolysis of intermediate colored products. The salt (0.2-0.4 g) was dissolved in 50-100 ml water and left for a day. The solution gradually grew lighter and took on a dark orange color. A precipitate slowly came down. The ether was extracted with benzene and the latter evaporated in air.

On hydrolysis of the addition product of iso- $C_3H_7OK$  to trinitroanisole we isolated the isopropyl ether of picric acid in a yield of 15%. M.p.  $92.0-92.5^\circ$ .

Found %: N 15.23.  $C_9H_9O_7N_3$ . Calculated %: N 15.50.

The addition products of trinitroanisole of tert- $C_4H_9OK$  and  $C_6H_5OK$  gave on hydrolysis 10 and 16% yields of the corresponding starting trinitroanisole. The addition product of sec-n- $C_8H_{17}OK$  hydrolyzed entirely to potassium picrate.

The intermediate colored products were also decomposed by a solution of sulfuric acid (1:10). The addition product of potassium tert-butyrate regenerated 70% trinitroanisole, and the addition products of potassium sec-n-octylate, 10% trinitroanisole.

On hydrolysis of the addition product of iso- $C_3H_7OK$  to the isopropyl ether of picric acid, and also of the addition product of tert- $C_4H_9OK$  to the isopropyl ether of picric acid, we isolated the initial ether with yields of more than 30%. Hydrolysis of the addition product of sec-n- $C_8H_{17}OK$  to the isopropyl ether of picric acid gave picrate.

Transesterification of 2,4-dinitroanisole by isopropyl, tert-butyl, and sec-n-octyl alcoholates. To a solution of 0.0005 mole of dinitroanisole in 10 ml of benzene was added a solution of 0.002 mole KOH in the corresponding alcohol. The solution became dark red. After standing for an hour 100 ml of water was added and the mixture was shaken in a separatory funnel. The benzene layer was washed three times with water and then the benzene was evaporated in air. In the reaction of dinitroanisole with potassium isopropylate we obtained the isopropyl ether with a yield of 75% (m. p.  $53.4-54^\circ$ ). In the remaining cases the starting dinitroanisole was regenerated quantitatively.

## SUMMARY

In the attempt at nucleophilic substitution of methoxy and isopropoxy groups in the corresponding ethers of 2,4-di- and 2,4,6-trinitrophenols by groups containing tert-butyl and sec-n-octyl radicals, the transesterification reaction did not occur, due to spatial hindrance.

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# REACTIONS OF AROMATIC NITRO COMPOUNDS

## X. A STUDY OF PRODUCTS OF THE YANOVSKII REACTION BY ABSORPTION SPECTRA

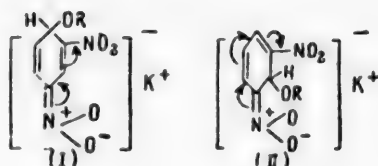
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In the reaction of *m*-dinitrobenzene and its derivatives with acetone in an alkaline medium, as we showed earlier [1], there are formed two series of derivatives, depending on the place of addition of the enol form of acetone.



In the absorption spectra of the products of the Yanovskii reaction the monosalt (I) corresponds to a short-wave maximum (550-573  $m\mu$ ) and monosalt (II) to a long-wave maximum (600-688  $m\mu$ ). The *m*-dinitrobenzene which we studied contained only methyl groups.

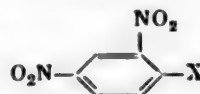
There is much interest in testing the results on *m*-dinitrobenzene derivatives with other substituents and in determining their effects on the shift of the absorption maximum in the complexes which are obtained.

### EXPERIMENTAL

All the polynitrocompounds which we studied were synthesized by us and then purified by repeated crystallizations. The constants of the starting compounds and the absorption maxima of the colored complexes are given in Table 1, and the absorption spectra of some of them are shown in Figs. 1-3. The method of obtaining the absorption spectra was described previously [1].

### DISCUSSION OF RESULTS

In the compounds studied with the general formula



positions 3 and 5 were not

occupied by any substituents and therefore it was possible to form complexes (I) and (II). If position 3 was substituted, then as a result of the Yanovskii reaction, complex (I) would form and in the absorption spectrum we would find the short-wave maximum, as, for example, in 1,2,4-trichloro-3,5-dinitrobenzene, and 3,4,5-trinitroxylylene. If position 5 was screened by any substituent, only complex (II) would form, as indicated by the presence

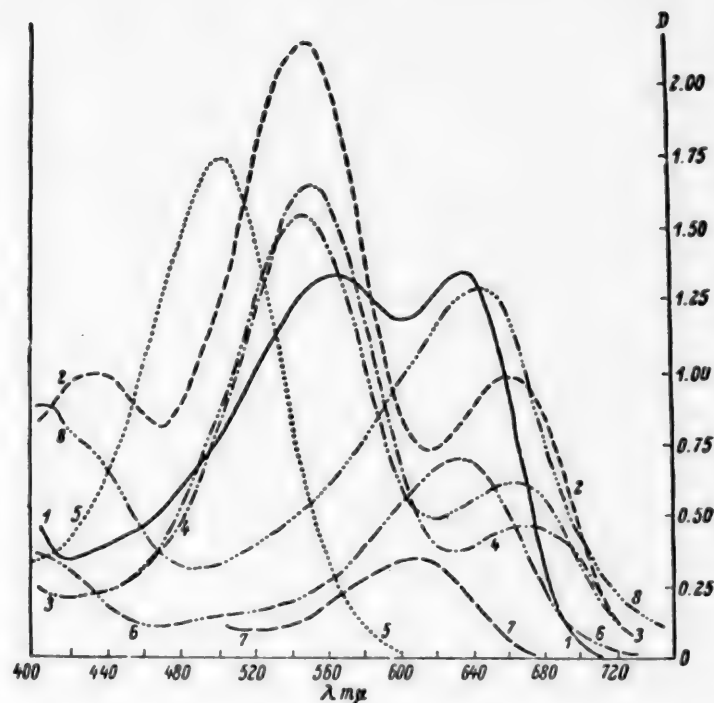


Fig. 1. Absorption spectra of products of the Yanovskii reaction for halogen derivatives of *m*-dinitrobenzene. 1) 2,4-dinitrofluorobenzene; 2) 2,4-dinitrochlorobenzene; 3) 2,4-dinitrobromobenzene; 4) 2,4-dinitroiodobenzene; 5) 1,3,6-trichloro-2,4-dinitrobenzene; 6) 1,5-dichloro-2,4-dinitrobenzene; 7) 1-chloro-5-fluoro-2,4-dinitrobenzene; 8) 1-methyl-5-bromo-2,4-dinitrobenzene.

of the long-wave maximum which we find in 1,3-dichloro-4,6-dinitrobenzene, 1,3-diethoxy-4,6-dinitrobenzene, 3-bromo-4,6-dinitrotoluene, and others. However, not for all of our compounds which had no substituent in positions 3 and 5 did we find two maxima in the absorption spectra of the Yanovskii reaction products. Thus, for example, for the ethyl ether of 2,4-dinitrophenol we found in the spectrum only a marked shift in the short-wave maximum with time: from 580 to 561  $m\mu$  after 35 minutes (Fig. 3). This shift can easily be explained by the disappearance in this time of products which have the long-wave absorption maximum. The long-wave maximum is superimposed on the short-wave one in such a way that the over-all maximum is first seen at 580  $m\mu$ . The assumed size of the long-wave maximum can be calculated if we accept that the shifts in absorption maximum caused by the different substituents are additive. Then, starting from  $\lambda_{\max}$  of the complex (II) for 5-ethoxy-2,4-dinitrotoluene and  $\lambda_{\max}$  for 2,4-dinitrotoluene (I), we can calculate the presumed position of the long-wave absorption maximum for the alkyl ethers of 2,4-dinitrophenol:  $\lambda_{\max}$  of dinitroanisole =  $\lambda_{\max}$  of dinitrotoluene -  $\lambda_{\max}$  of 5-ethoxy-2,4-dinitrotoluene = 662  $m\mu$  - 600  $m\mu$  = 62  $m\mu$ . Hence, the introduction of an ethoxy group leads to a hypsochromic shift of the long-wave absorption maximum by 62  $m\mu$  and its wave length for alkyl ethers of 2,4-dinitrophenol should be less than in *m*-dinitrobenzene by 62  $m\mu$ , that is, 688  $m\mu$  - 62  $m\mu$  = 626  $m\mu$ . The introduction of a second diethoxy group (1,5-diethoxy-2,4-dinitrobenzene) gives a hypsochromic shift of the long-wave maximum of 73  $m\mu$  (626  $m\mu$  - 553  $m\mu$  = 73  $m\mu$ , where 553  $m\mu$  is the  $\lambda_{\max}$  of the diethoxy derivative). Using these values we can calculate the wavelength of the corresponding maxima for the short-lived complexes of *m*-dinitrobenzene derivatives. Not all the *m*-dinitrophenol ethers have only one stable absorption maximum. Thus, in the case of the phenyl and trifluoromethyl ethers of 2,4-dinitrophenol both maxima are clearly visible in the corresponding spectra (see Fig. 2).

In 2,4-dinitroaniline, 2,4-dinitrophenylhydrazine, and 2,4-dinitrophenylhydroxylamine, just as in the alkyl ethers of 2,4-dinitrophenol, only the short-wave maximum is seen clearly (see table). However, they have the comparatively short-lived complex (II), and this shows a marked shift to the short-wave part of the spectrum. Thus, for example, for dinitrophenylhydrazine  $\lambda_{\max}$  is shifted after 30 minutes from 605 to 570  $m\mu$ .

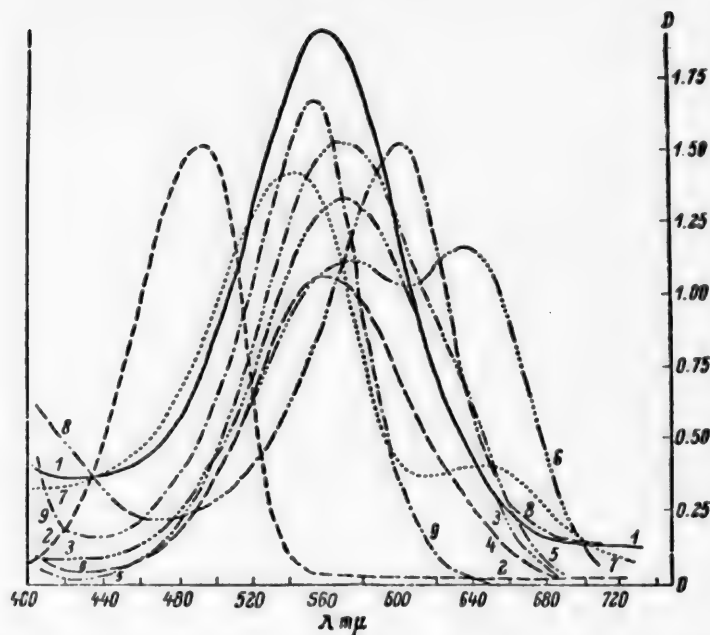


Fig. 2. Absorption spectra of products of the Yanovskii reaction for alkoxy- and aryloxyderivatives of *m*-dinitrobenzene. 1) 2,4-dinitroanisole; 2) glycol ether of 2,4-dinitrophenol; 3) allyl ether of 2,4-dinitrophenol; 4) furfuryl ether of 2,4-dinitrophenol; 5) benzyl ether of 2,4-dinitrophenol; 6) phenyl ether of 2,4-dinitrophenol; 7) trifluoromethyl ether of 2,4-dinitrophenol; 8) 5-ethoxy-2,4-dinitrotoluene; 9) 1,5-diethoxy-2,4-dinitrobenzene.

These results show that the radical X has a marked effect on the ability of the dinitro compounds to form complexes. The formation of complex (II) evidently depends on the electron-donor ability of the radicals. Those radicals which increase the electron density in the benzene ring decrease  $\delta^+$  on carbon atoms 3 and 5, which makes the addition of acetone enol difficult. If we consider the spacial hindrance created by two neighboring nitro groups on the entrance of acetone enolate in the 3 position it becomes clear why formation of complex (II) is difficult.

On the basis of the data on value of the replacement constant  $\sigma_{\text{meta}}$  [2] the substituents studied can be arranged in the following order with respect to decreasing electron-donor ability:



Our results show that the formation of complex (II) depends on the size of  $\sigma_{\text{meta}}$ . Beginning already with the alkoxy group, the electron-donor power of the substituents becomes sufficient to hinder formation of complex (II). Decrease in donor ability of the OR group due to introduction in place of the alkyl radical of the electrophilic groups  $\text{C}_6\text{H}_5$  and  $\text{CF}_3$  leads to increased stability of the complex and the long-wave maximum is observed in the absorption spectrum. The presence of a substituent which stands to the left of the alkoxy group leads to absence of the long-wave maximum in the spectra of the products of the Yanovskii reaction. The carboxyl group, as is known, is an electron acceptor, but in the conditions of forming the complexes (alkaline medium) 2,4-dinitrobenzoic acid gives a stable anion  $(\text{NO}_2)_2\text{C}_6\text{H}_3\text{C}(=\text{O})\text{O}^-$ , in which the  $-\text{C}(=\text{O})\text{O}^-$  group has strong elec-

tron-donor properties. These groups, like a negatively charged oxygen atom in 2,4-dinitrophenolate fully deactivate carbons 3 and 5 of the benzene ring, so that they cannot form the colored complexes (I) and (II) at all.

These results show that the position of maximum absorption of the dinitro derivative complexes, formed as the result of the Yanovskii reaction, does not remain constant. The change in position of both maxima permits

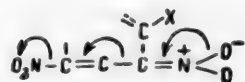
TABLE 1

Name of compound	M. p.		Short wave maximum		Long wave maximum	
	our data	literature data	$\lambda'_{\max}$	$\Delta\lambda'_{\max}$	$\lambda''_{\max}$	$\Delta\lambda''_{\max}$
2,4-Dinitrofluorobenzene	24°	24.3° [6]	562	11	633	55
2,4-Dinitrochlorobenzene	52.5—53	53.4 [6]	548	25	660	28
2,4-Dinitrobromobenzene	75	75.3 [6]	545	28	663	25
2,4-Dinitroiodobenzene	87.5	88.5 [6]	550	23	672	16
1,3,6-Trichloro-2,4-dinitrobenzene	102—103	103.5 [6]	505	68	—	—
1,5-Dichloro-2,4-dinitrobenzene	102	103 [6]	—	—	634	54
1-Chloro-5-fluoro-2,4-dinitrobenzene	76	76 [6]	—	—	610	78
5-Bromo-2,4-dinitrotoluene	104	103—104 [6]	—	—	647	41
Dinitroanisole	94.5—94.8	88.6 [9]	560	13	626*	62*
Dinitrophenetole	85.5—86	86.5 [9]	561	12	625*	63*
Isobutyl ether of 2,4-dinitrophenol	31	30.3—31.5 [7]	570	3	—	—
Benzyl ether of 2,4-dinitrophenol	149—150	149.5 [8]	560	13	—	—
Phenyl ether of 2,4-dinitrophenol	71	71 [8]	571	2	638	50
Glycol ether of 2,4-dinitrophenol	111.4	111—112 [9]	493	80	—	—
Allyl ether of 2,4-dinitrophenol	47	46—47 [8]	570	3	—	—
Trifluoromethyl ether of 2,4-dinitrophenol**	—	—	545	28	647	41
5-Methoxy-2,4-dinitrotoluene	101	101—101.5 [10]	—	—	598	90
5-Ethoxy-2,4-dinitrotoluene	95—96	95—96 [10]	—	—	600	88
1,5-Diethoxy-2,4-dinitrobenzene	132	133 [10]	—	—	552	116
Furfuryl ether of 2,4-dinitrophenol	131—32	—	558	15	—	—
Dinitroaniline	186	188 [6]	522	51	—	—
Dinitrophenylhydrazine	195	197 [6]	—	—	570	3
Dinitrophenylhydroxylamine	80 (dec.)	80 [11] (dec.)	490	83	—	—
1,2,4-Trinitrobenzene	57	57.5 [11]	528	45	656	32
3,4,5-Trinitro-o-xylene	115—116	115 [6]	558	15	—	—
3,4,6-Trinitro-o-xylene	71	72 [6]	—	—	575	113
2,4-Dinitrophenol	114	114—115 [6]	—	—	—	—
2,4-Dinitrobenzoic acid	178—179	179 [6]	—	—	—	—

\* Calculated by us.

\*\* First synthesized by L. M. Yagupol'skii and kindly supplied to us for study.

us to explain the effect of the different substituents on the spectral behavior of the complex and to establish the relative strength of action of the different substituents. Substituent X which occurs in the ortho and para positions to the nitro groups stands outside the conjugated chain in monosalt (I), and in monosalt (II) it is directly bound to the carbon atoms of the conjugated chain. The conjugated chain of complex (I) (short-wave maximum) can be represented schematically thus,



For m-dinitrobenzene, that is, when X = H,  $\lambda_{\max} = 573 \text{ m}\mu$ . Replacement of the hydrogen atom by different electron donors and electron acceptors as substituents leads to a shift in the absorption maximum toward the short-wave part of the spectrum. The relative strength of action of the substituents can be characterized by the value for  $\Delta\lambda_{\max}$  which is the difference in absorption maxima of the corresponding complexes of m-dinitrobenzene and its derivatives:  $\Delta\lambda_{\max} = \lambda_{\max} \text{ 2,4-dinitrobenzene} - \lambda_{\max} \text{ 1-X-2,4-dinitrobenzene}$ .

Comparison of the data shows that the shift in absorption maxima of complex (I) occurs in relation to the electron-donor strength of the substituent, that is, the greater or lesser ability to shift the electron density in the direction of the conjugated chain. Actually, when  $X = \text{CH}_3$ ,  $\text{OC}_6\text{H}_5$ ,  $\text{OCH}_2\text{CH}=\text{CH}_2$ , the shift in maxima is very slight. Alkoxy groups shift the absorption maxima by 10-13  $\text{m}\mu$ , and halogens by 11-30  $\text{m}\mu$ . In a number of halides there is a regular shift of  $\lambda_{\text{max}}$  depending on the value of  $\sigma_{\text{meta}}$  (see the following table).

Halide	F	Cl	Br	I
$\sigma_{\text{meta}}^{[2]}$	0.317	0.373	0.391	0.352
$\Delta\lambda_{\text{max}}$	11	25	28	23

A still sharper shift occurs in compounds with great electron-donor capacity.

R	$\text{NH}_2$	<	$\text{OCH}_2\text{CH}_2\text{O}^-$	<	$\text{NHIO}^-$
$\Delta\lambda_{\text{max}}$	51		80		83

As the data which have been given show, increase in electron-donor capacity of the substituents connected to the conjugated chain through two single bonds increases the hypsochromic shift of the absorption maxima. The electron-accepting nitro groups of 1,2,4-trinitrobenzene by their negative inductive effect decrease the oscillation of the charge in the conjugated chain, so that there is a marked hypsochromic shift.

The conjugated chain of complex (II) (long wave maximum) has the form:  $\text{O}_2\text{N}=\text{C}=\text{C}=\text{C}-\text{C}(\text{X})=\text{C}=\text{C}-\text{NO}_2$

In this case, X is located directly on a carbon atom of the conjugated chain. The approach of the substituent to the conjugated chain leads to an increased effect of it on the absorption spectrum of the compound. Thus, if in complex (I) the introduction of a methyl group leads to a shift of  $\lambda_{\text{max}}$  of 1  $\text{m}\mu$  [1], then for complex (II) the shift is 26  $\text{m}\mu$ . The substituent in this case competes with the negative  $\text{O}^--\text{N}^+-\text{O}^-$  group for conjugation with the positive nitro groups which are acceptors in the conjugated chain. The reaction of the substituents with the acceptor nitro group occurs through the conjugated chain which is shown schematically by the dotted line. The stronger this reaction, the less the share of this nitro group in the conjugation with the others which are electron donors. Such an action of the substituent is equivalent to "shortening" the conjugated chain and should be shown in a hypsochromic shift of the absorption maximum. Evidently in this case the effect of the substituent on the shift of the absorption maximum should depend on the size of its positive effect of conjugation. Actually, all the substituents studied can be arranged according to the value of the maxima in an order which agrees well with some of the results in the literature on the strength of the +C effect [3].

X	$\text{OCH}_3 \sim \text{OC}_2\text{H}_5 \sim \text{OC}_4\text{H}_9$	>	$\text{OC}_6\text{H}_5$	>	$\text{OCF}_3$ ; F	>	Cl	>	Br	>	I	>	H
$\Delta\lambda_{\text{max}}$	64		50		41 55		28		25		16		0

The effect of a methyl group on the shift depends on the appearance in the given case of  $\sigma, \pi$ -conjugation [4]. As a result of this, the methyl group shows about the same electron-donor properties as the bromine. The nitro group shifts the absorption maximum of complex (II) by 32  $\text{m}\mu$ . Its electron-acceptor action leads to shortening of the conjugated chain, which is also shown in the hypsochromic shift.

It should be noted that when still another substituent, X', is introduced into the conjugated chain in position 3 its reciprocal effect leads to a decrease in  $\lambda_{\text{max}}$  of about the same value as this substituent shifts the absorption maximum in the monosubstituted complex. Thus, in 4,6-dinitro-m-xylene for each methyl group there is a  $\Delta\lambda_{\text{max}} = 21.5 \text{ m}\mu$ , while the methyl group in 2,4-dinitrotoluene shifts the maximum by 26  $\text{m}\mu$ ; in 1,3-dichloro-4,6-dinitrobenzene,  $\Delta\lambda_{\text{max}}$  for each chlorine atom is 27  $\text{m}\mu$ , which agrees well with  $\Delta\lambda_{\text{max}}$  for 2,4-dinitrochlorobenzene (28  $\text{m}\mu$ ). An analogous effect is found in 1-chloro-3-fluoro-4,6-dinitrobenzene where the total shift from the action of the halogen atoms in the complex is 78  $\text{m}\mu$ , where  $\Delta\lambda_{\text{max}}$  of chlorine is 28  $\text{m}\mu$ , of fluorine 50  $\text{m}\mu$  ( $\Delta\lambda_{\text{max}}$  in 2,4-dinitrofluorobenzene is 55  $\text{m}\mu$ ).

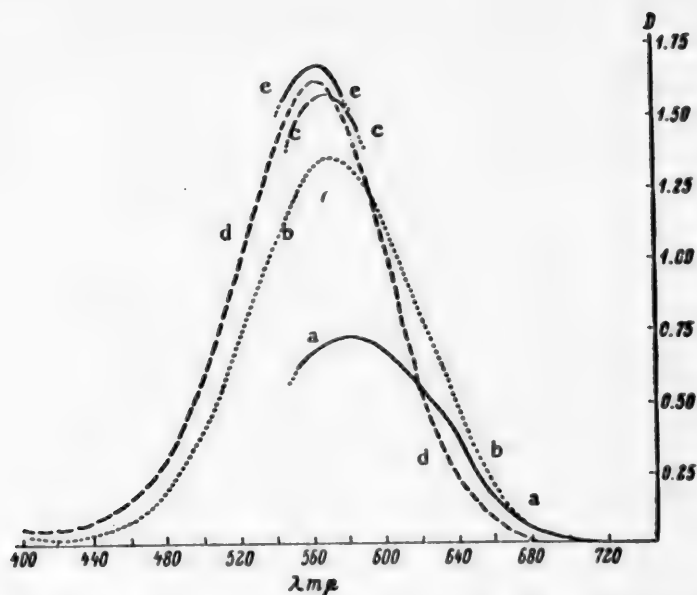


Fig. 3. Shift in absorption maxima of a complex of 2,4-dinitrophenol with time. a) After 1 min from the moment of formation; b) after 2 min; c) after 3 min; d) after 7 min; e) after 35 min.

The values obtained by Newlands and Wild [5] for the absorption maxima of some 2,4-dinitrobenzene derivatives agree well with our results. However, they did not succeed in observing in the absorption spectrum the short-lived long-wave maxima. The short-wave absorption maxima (430 mμ) observed by these authors in 2,4-dinitrofluorobenzene comes from the decomposition products of the complex. We also found formation of the latter in some cases, and its amount increased with rising temperature or addition of water.

#### SUMMARY

1. We have photographed the absorption spectra of the complexes formed in the reaction of derivatives of m-dinitrobenzene with acetone in an alkaline medium.
2. We have showed that derivatives of m-dinitrobenzene tend to form complexes of the type of monosalt (I) and monosalt (II), that is, the results of the investigation confirm our previous data on the structure of the complexes.
3. We have studied the effect of electron-donor and electron-acceptor substituents on the absorption maxima of the colored complexes. The action of substituents separated from the conjugated chain by two ordinary bonds depends on their electron-donor capacity. The effect of substituents directly connected with the conjugated chain depends on their conjugation effect.

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## STUDIES IN THE FIELD OF VAPOR-PHASE CATALYTIC HYDRATION OF ACETYLENE AND ITS DERIVATIVES

### VII. STUDY OF COPPER-CALCIUM PHOSPHATE CATALYSTS

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From the literature and patent data [1-4] it is known that some salts of Cu, Cd, Zn, and Hg are catalysts for the reaction of addition of water to acetylene. This catalytic property is probably connected with the specific structure of the electron shells of these elements [4]. Copper phosphate is used as an active additive to various contact substances in whose composition phosphoric acid occurs or to zinc phosphate, and as carriers activated charcoal or cuprene [5-7] are used. There is information on the use of copper salts without a carrier [8].

We have set ourselves the problem of studying the action of copper phosphate and various other copper salts as agents which produce the hydration of acetylene. As a second component of the catalyst we have chosen calcium phosphate in connection with the information [9] on the greater stability of contact substances prepared with its use as the carrier. We have prepared and studied catalysts of copper phosphate and also various mixtures of it with calcium phosphate. The results of the study of the catalytic activity are shown in the table.

The addition to calcium phosphate, which in itself has no activity, of 0.01% cupric phosphate at once produces a marked effect which is gradually strengthened as the addition is increased, and which reaches a maximum at 0.3%.

Further increase in the amount of cupric phosphate causes loss of activity. The catalyst which contains about 1% cupric phosphate is distinguished by very high selectivity and activity. At 10% cupric phosphate in the catalyst and especially with cupric phosphate alone there is a sharp fall in yield of aldehyde and formation of a large amount of tarry products and cuprene which leads to clogging of the reaction tube and necessitates stopping the reaction.

It is of interest to explain how the form of the calcium phosphate affects the activity of the copper-calcium phosphate catalyst. For this purpose we prepared a number of catalysts in which 0.1% cupric phosphate was added to a mixture of tri- and dicalcium phosphates of different compositions. The results of the study of these catalysts showed that the activity of the catalyst is higher the greater the content in the carrier of neutral orthophosphate. We should remark that the gradual decrease in activity during 25 hr of work (samples taken and control analysis run each six hr during the experiment) was more marked in catalysts which contained much of the acid salt. Therefore the average activity after 25 hr was higher for the samples which consisted briefly of neutral calcium phosphate (although in the first hr, on the contrary, the catalysts which contained considerable amount of acid phosphate worked more actively). The greater stability of these catalysts was evidently connected with the fact that when the neutral orthophosphate was heated it did not undergo any sort of change. The fall in activity of the forms with a high content of acid phosphate was probably related to the change of the latter into pyrophosphate which was observed roentgenographically in the spent copper-calcium phosphate catalysts which originally contained acid calcium orthophosphate. One of the reasons for the lower activity of the catalysts

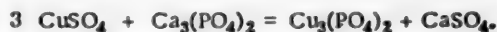
Effect of Content of Cupric Phosphate on the Activity of Copper-Calcium Phosphate Catalysts (Volume rate of  $C_2H_2$  200 liters/liter catalyst/hour,  $C_2H_2 : H_2O = 1 : 10$ ; length of experiment 6 hr)

No.	Content of cupric phosphate in catalyst, %	Temperature	Amount of conversion of $C_2H_2$ , %	Yield of aldehyde (mole%)		Productivity of catalyst based on aldehyde (g/liter catalyst/hr)
				on $C_2H_2$ passed	on $C_2H_2$ reacting	
1	0.00	450°	Not determined	1	—	6
2	0.01	450	48	46	95	130
3	0.07	390—400	65	62	96	240
4	0.1		80	75	94	300
5	0.3		86	82	96	312
6	1.0		75	72	97	280
7	10.0	150—300	70	41	58	150
8*	100.0		66	24	37	210

\* Mole ratio of  $CuO : P_2O_5$  in catalyst No. 8 was 3.1 : 1; the volume rate of acetylene was 500 liter/liter of catalyst/1 hr; length of experiment was 1 hr.

which contained the acid phosphate (pyrophosphate) might be the lower specific surface of the latter compared to the neutral orthophosphate. The specific surface of neutral calcium orthophosphate is  $102 \text{ m}^2/\text{g}$ , while for pyrophosphate it is  $9 \text{ m}^2/\text{g}$ .

For a study of the effect on the activity of the copper-calcium phosphate catalyst of the nature of the starting copper compound we took different salts of mono and divalent copper (in the amount of 0.13%), metallic copper and copper hydroxide (0.35%). As the carrier we used neutral calcium phosphate and its mixtures with acid phosphate. The results of the study of the catalysts showed that (with the exception of samples prepared with cuprous chloride and metallic copper) the nature of the starting copper salt did not have much significance.\* It is not impossible that in the process of preparing the catalyst and its use at high temperatures, as a result of exchange reactions with the excess calcium phosphate (independent of the anion of the starting copper salt), cupric phosphate is formed. Actually it was shown that in preparing the catalyst with use of cupric sulfate there was an exchange reaction:



The catalyst which contained cupric hydroxide also had considerable activity (yield of aldehyde 40–50%). We can assume that here also there occurs reaction of the cupric hydroxide with calcium phosphate with formation of cupric phosphate. The same thing can also be assumed for catalysts which contain metallic copper and cuprous chloride.\*\* However, the reaction with calcium phosphate in these last two cases evidently occurs more slowly and less completely and this explains the lower activity of these catalysts: the yield of aldehyde on the acetylene passed was on the order of 15–20%.

On the other hand, in previous communications [4, 10], it was shown that the activating action on acetylene of different cadmium salts, produced by ions of crystals, depended on the effect of the cation and was almost independent of the nature of the anion. Therefore it is very probable that the reason for the almost identical activity of catalysts prepared with different copper salts is the activity of the copper cation, independent of what anion was added to the catalyst.

The stability of the copper-calcium phosphate catalysts. The copper-calcium phosphate catalysts were studied for deactivation in long continued work. The study was carried out in an enlarged experimental apparatus; we compared two forms of catalyst prepared by different catalysts. One form (I) was prepared by mixing

\* The yields of aldehyde were about 50% (on the acetylene passed).

\*\* Compounds of monovalent copper probably do not catalyze the process of vapor-phase hydration of acetylene [4, 5]. The small effect produced by this catalyst can depend on partial conversion of monovalent copper to divalent.

suspensions of cupric phosphate and calcium phosphate. The ratio of  $\text{CaO} : \text{P}_2\text{O}_5$  in the calcium phosphate was 3:1, the content of cupric phosphate was 0.14%. The second catalyst (II) was prepared by adding a solution of cupric acetate to a suspension of calcium phosphate with strong stirring. This method of preparation permitted an even addition of cupric phosphate on the surface by the exchange reaction. The ratio of  $\text{CaO} : \text{P}_2\text{O}_5$  was 2.8:1, the content of cupric phosphate was 0.1%. The results of the study of these catalysts showed that the length of one cycle of contacting on catalyst II of 100 hr exceeded the cycle of contacting on catalyst I (about 50 hr) more than twofold. The temperature of contacting on catalyst II averaged somewhat lower (360-390°) than in the experiments on catalyst I (400-410°). Exhaustion of catalyst II began to appear after 600 hr of work, while for catalyst I it became marked even after 300 hours.\* Thus, the second method of preparation gives increased activity and stability to the copper-calcium phosphate catalyst.

## EXPERIMENTAL

Preparation of calcium phosphate, cupric phosphate, and the copper-calcium phosphate catalyst. Calcium phosphate was precipitated from a solution of calcium acetate with dibasic ammonium phosphate. The precipitate was washed and dried at 100-110°. After grinding and sifting through a fine sieve, the powder was pressed into tablets with a hand hydraulic press. The tablets were broken up into pieces with a diameter of 2-4 mm.

Cupric phosphate was precipitated by pouring together streams of solutions of cupric sulfate and dibasic ammonium phosphate. The precipitate was washed free of sulfate ions, filtered, dried to constant weight at 100-110° and pressed into tablets. The molar ratio  $\text{CuO} : \text{P}_2\text{O}_5$  was 3.1:1.

For the preparation of the copper-calcium phosphate catalyst with differing copper contents, 100 g of the dry powder of calcium phosphate was suspended in 1.5 liters of a solution which contained the required amount of copper sulfate. The solution of ammonium phosphate was added evenly to the solution. The filtered catalyst mass was dried at 100-110° and pressed into tablets.

Preparation of copper-calcium phosphate catalysts with different  $\text{CaO} : \text{P}_2\text{O}_5$  ratios. The preparations of calcium phosphate were precipitated from solutions of calcium chloride by dibasic ammonium phosphate to which differing amounts of ammonia had first been added. The introduction of cupric phosphate was carried out by the method described above. The catalyst was pressed into tablets.

Preparation of catalyst using different copper salts. Copper vanadate and iodide were prepared by the action on a solution of copper sulfate of solutions of ammonium vanadate and potassium iodide. The washed precipitate of copper salt was suspended in a small amount of water and carefully mixed with a suspension of calcium phosphate. Further operations in the preparation of the catalyst were carried out as described above.

The introduction of copper acetate and sulfate was carried out by suspending the dry powder of calcium phosphate in solutions containing the calculated amount of the corresponding copper salt.

The catalyst with metallic copper was prepared by mixing the dry calcium phosphate powder with finely dispersed metallic copper obtained by displacement from a copper sulfate solution with powdered iron.

The catalysts with cupric hydroxide and cuprous chloride were prepared by mixing the dry calcium phosphate powder and the copper compound, followed by pressing into tablets. The catalyst which contained the cuprous salt, before study of its activity, was kept under nitrogen which contained no impurity of oxygen.

Preparation of the catalysts used in the experimental apparatus. Catalyst I was prepared by mixing a suspension of cupric phosphate with a suspension of freshly precipitated and washed calcium phosphate. The catalyst mass was filtered and formed into "worms" by forcing through a plate with 4 mm openings. After drying at 100-110° the worms had a diameter of 2.5 mm and had good mechanical strength. Catalyst II was prepared by gradually adding a solution of cupric acetate to a suspension of freshly precipitated and washed calcium phosphate with intensive stirring with a mechanical stirrer. The further operations of filtering, forming into worms, and drying did not differ from those for catalyst I.

All the catalysts were analyzed for their content of Cu, CaO, and  $\text{P}_2\text{O}_5$ . Calcium was precipitated as the oxalate and determined by titration with 0.1 N  $\text{KMnO}_4$  solution [11]. Phosphoric acid was converted to ammonium phosphomolybdate with later titration of the precipitate by 0.5 N solution of alkali [12]. The copper content was determined by electrolysis [13]. For determination of the loss in ignition the sample of catalyst was heated in a crucible furnace at 800° to constant weight.

\* The amount of conversion of acetylene was about 50%, with a yield of aldehyde on reacting acetylene of about 90%.

The surfaces of the neutral calcium orthophosphate and the calcium pyrophosphate were determined by low temperature adsorption of nitrogen [14].

The activity of the catalyst was studied on a laboratory apparatus [7]: the volume of the catalyst in the reaction tube was 50 ml. For this work we used acetylene from a cylinder with a content of  $C_2H_2$  of 99%, purified from admixtures by passage through a system of absorbers with solutions of sodium hypochlorite. The content of acetylene in the gas entering the furnace and also in the reaction gas was determined by absorption in oleum in an Orsat apparatus. We determined the aldehyde content in the water condensate with hydroxylamine hydrochloride.

The study of the activity and stability of the copper-calcium phosphate catalysts I and II was carried out in an experimental contact apparatus whose construction was analogous to that of the laboratory apparatus, but because of greater capacity of the gasometer could be used for long experiments without interruption. After a cycle of contacting, regeneration of the catalyst was carried out in a stream of mixed air and steam at 400-450° until  $CO_2$  disappeared from the outgoing gas. The length of regeneration of catalyst I was 12-15 hr; regeneration of catalyst II took about 40 hr.

#### SUMMARY

1. We have showed that the addition of 0.1-0.3% cupric phosphate to calcium phosphate gives a highly active and selective catalyst for the hydration of acetylene.
2. We have established the relation between activity of the copper-calcium phosphate catalyst and ratio of neutral and acid phosphates of calcium in it. We have showed that the most active and stable catalysts are those whose composition approaches that of neutral calcium orthophosphate.
3. The use of different salts of divalent copper as additives (0.1-0.3%) to the calcium phosphate produces almost the same effect as the equivalent addition of cupric phosphate. The activity of the catalysts prepared with metallic copper or cuprous chloride is slight.
4. On copper-calcium phosphate catalysts under corresponding conditions of preparation it is possible to carry out hydration of acetylene for about 100 hr with a total length of working of the catalyst of 600 hr.

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## STUDIES IN THE FIELD OF VAPOR-PHASE CATALYTIC HYDRATION OF ACETYLENE AND ITS DERIVATIVES

### VIII. THE ROLE OF THE CARRIER IN THE TWO-COMPONENT CATALYST FOR HYDRATION OF ACETYLENE TO ACETALDEHYDE

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In previous communications [1-3] we considered the problem of the possible scheme of vapor-phase hydration of acetylene and its derivatives on solid ionic catalysts, the relation of the activity of the latter to the structure of the electron shell of the cations, and the influence of the anions on the character of this process; here we considered only one side of the reaction, namely, the activation of the acetylene under the action of the catalyst. The possibility of the reaction of the catalyst with the other component of the reaction, the water, was not discussed by us in these papers. The few investigators who have studied the mechanism of vapor-phase hydration of acetylene [4-6] have directed their attention exclusively to the reaction of the catalyst with acetylene and the further transformations of the first-intermediate product of addition of water to acetylene. Evidently the opinion is established that, under the conditions of the catalytic process in the vapor phase, addition of water to acetylene occurs without action of the catalyst on it. However, the experimental data which we have obtained in studying the activity of different two-component phosphate catalysts shows that this step of the process probably occurs with participation of the catalyst.

It is known from patents [7] that the use of calcium phosphate mixed with cadmium phosphate permits obtaining a very active catalyst. Our studies [8] have established that good results are also obtained by combining calcium phosphate with cupric phosphate. Since it has also been shown that calcium phosphate by itself has no activity, we originally assumed that its role in the two-component catalyst was to create a more developed surface for the active phosphate (the specific surface of neutral cadmium orthophosphate is  $10-12 \text{ m}^2/\text{g}$ , and of neutral calcium orthophosphate, about  $100 \text{ m}^2/\text{g}$ ). Since we wished to determine the possibility of giving the catalyst a large surface, with other carriers, we used in combination with the active phosphate activated charcoal and calcined silica gel. We also used pumice which had a small specific surface.

We studied two sets of catalysts: for one, as the agent for activating acetylene, we used cupric phosphate, for the other cadmium phosphate. In view of the high activity of cupric phosphate [8] we added 0.15% (by weight) to the catalyst. The content of cadmium phosphate in our mixed catalysts was 15-16%.

It was also of interest to test whether the ability to serve as a good carrier for the active phosphate was a specific property of calcium phosphate, or other phosphates were suitable for this purpose. As such we studied the phosphates of strontium [7] and barium, in which we had previously shown the absence of intrinsic catalytic activity [2]. The results of the study of the two-component phosphate catalysts (with different carriers) are shown in the table.

These data show that not only calcium phosphates, but also the phosphates of the other alkaline earth metals combined with copper or cadmium phosphate give active catalysts. When the phosphate carrier is replaced with pumice, carbon, or silica gel, the activity of the contact substances is sharply reduced, especially in the case of



the cupric phosphate where there occurs a side reaction of polymerization of acetylene into cuprene and other products; the deposit of cuprene was obviously visible in the spent catalyst. Some side reactions were also found on those catalysts for which the carrier was strontium or barium phosphate, but these had the character of secondary processes, condensation of the aldehyde after formation into oily products.

These results lead us to conclude that the role of the catalyst in the process of vapor-phase hydration of acetylene is more complex than it would seem at first glance. The high activity of catalysts consisting of cupric phosphate on phosphates of the alkaline earth metals indicates that a small amount of cupric phosphate is entirely sufficient for activation of acetylene. However, the absence of reaction on catalysts consisting of the same amount of copper phosphate mixed with pumice, carbon, or silica gel gives us a reason to suppose that the activation of acetylene is not the only condition for the occurrence of its hydration. It is possible that particles of the water which react also should be brought into an active state. In such a case, the catalyst of the vapor-phase hydration of acetylene should be fulfilling a double function.

Effect of the Carrier on Activity of Phosphate Catalysts (Volume rate  $C_2H_2$  150 liters/liter catalyst/hour; temperature 390-400°, dilution  $C_2H_2:H_2O = 1:10$  mole)

Active phosphate	Carrier	Length of experiment (hrs)	Amount of conversion of acetylene, %	Yield of acetaldehyde, mole %		Specific surface of catalyst ( $m^2/g$ )
				on $C_2H_2$ passed	on $C_2H_2$ reacting	
Cupric phosphate, 0.15%	Neutral orthophosphate of:					
	calcium ..	10	65.6	56.0	85.4	94
	strontium. .	10	68.2	51.4	75.5	61
	barium . . .	10	52.7	41.2	78.1	—
	Pumice. . . .	3	2.2	2.0	88.5	5
	Activated					
Cadmium phosphate, 16%	charcoal . . .	3	5.1	1.3	25.5	800
	Silica gel	3	5.6	2.2	38.9	340
	Neutral orthophosphate of:					
	calcium ..	10	66.6	55.3	83.0	93
	strontium. .	10	76.5	61.8	80.7	48
	Pumice. . . .	10	21.3	15.7	72.6	6
	Silica gel . . .	10	14.1	10.4	72.6	265

Copper phosphate and cadmium phosphate, which are active hydration catalysts evidently have the ability to activate both acetylene and water. However, under the influence of cupric phosphate, activation of acetylene proceeds much more intensely than activation of water, so that the hydrating properties of cupric phosphate are suppressed by the processes by which it stimulates polymerization of acetylene with formation of cuprene [2, 8]. Cadmium phosphate activates acetylene much more weakly than does cupric phosphate (about 100 times, as the data of the table show), not causing any notable polymerization. Therefore the hydration process on cadmium phosphate goes much more smoothly.

Since in the case of the two-component catalyst with phosphate carriers an important amount of activation of acetylene is attained in the presence of 0.15 weight % of cupric phosphate and no reaction of polymerization occurs here, we must assume that the phosphates of calcium, barium, and strontium carry out here the second function of the hydration catalyst, the activation of water. The two-component cadmium phosphate catalyst acts in an analogous way, with this difference, that to reach an equal effect cadmium phosphate must be added to the catalyst in much greater amount.

On the other hand, pumice, activated charcoal, and silica gel evidently do not have the ability to activate water. Therefore the phosphate catalysts which contain such carriers are inactive (in this case the cadmium catalyst is more active than copper, since cadmium phosphate was added in greater amount which assures the possibility of some activation of water).

We have also tested the possibility of using calcium phosphate as a carrier for cadmium hydroxide, which itself is little active in the process of hydration of acetylene [3], and we are convinced that the activity and



selectivity of the two-component catalyst are incomparably higher than for cadmium hydroxide alone. Evidently here also because of the calcium phosphate there are created better conditions for activation of water.

The question arises, what is the character of this "activation"? On the one hand, it can be ascribed only to better adsorption of water on the phosphates so that contact is made easy for the water molecules with the activated acetylene molecules, while on the carrier which has less hydrophilic properties this does not occur. On the other hand, the process can be more complex. We suggest that the adsorbed water should undergo a further polarization which would raise its reactivity. The polarized water particles react with the polar or ionized acetylene complex from the cation of the catalyst which is in the immediate neighborhood [1, 2] to form the aldehyde (through the vinyl alcohol) and to regenerate the cation. Polarization of the water can evidently occur only under the influence of compounds which have an ionic lattice, as, for instance, phosphates of copper, cadmium, calcium, etc. The carrier, whose surface is more electroneutral, like pumice, a mixture of fused silicates [9], and calcined silica gel [10] or charcoal, whose lattices have partial covalence, as is known, and a partial metallic character, does not cause polarization of water. These substances cannot be used as carriers. The size of specific surface of these substances actually has no significance for the activity of the catalysts. The varying catalytic activity of different cadmium salts [3] can also be explained from the point of view of the greater or lesser ability of these compounds to adsorb water or cause its further polarization.

## EXPERIMENTAL

Neutral orthophosphates of cadmium, calcium, strontium, and barium which entered the composition of the catalysts were obtained by precipitation from the corresponding nitrates by the action of ammonium phosphate on them.

The two-component cadmium catalysts were prepared by careful mechanical mixing of the finely ground components. The weight content of cadmium phosphate in the catalyst was 15-16 weight %.

The copper catalysts on phosphate carriers were prepared by precipitation of cupric phosphate on finely ground phosphates of calcium, strontium, and barium suspended in a weak aqueous solution of cupric nitrate or sulfate. With mechanical stirring we added the stoichiometric amount of ammonium phosphate in the form of a dilute solution. The suspended catalyst was filtered off, dried, and pressed into tablets.

The copper catalysts on pumice, silica gel, and activated charcoal were prepared by precipitating cupric phosphate on the grains of the carrier which had first been impregnated with a solution of cupric nitrate or sulfate and then immersed in a solution of ammonium phosphate, after which they were separated from the liquid and dried. The amount of cupric phosphate on the carrier was about 0.15%. The catalysts were analyzed for copper content by electrolysis, for which the copper salt was extracted from the sample of catalyst with nitric acid.

The experiments on hydration of acetylene were carried out at 390-400°, volume rate of acetylene 150 liters/liter catalyst/hour and molar dilution of it by water 1:10. The description of apparatus, method of procedure, and analysis of the products were given previously [2]. We placed 50 ml of catalyst with grain diameter 3 mm in the reaction furnace. The length of the periodic experiments was 3-5 hr, the number of experiments on each sample differed depending on the activity of the catalyst. Regeneration of the catalyst between experiments was not carried out.

Determination of the specific surface of the catalysts was carried out with low-temperature adsorption of nitrogen [11].

## SUMMARY

1. We have showed that such substances as charcoal, calcined silica gel, and pumice, whose surfaces evidently have an electroneutral character, cannot be used as carriers in the catalytic vapor-phase hydration of acetylene. The phosphates of the alkaline earth metals, which are ionic crystals, are good carriers for these catalysts.

2. The activity of the catalysts for vapor-phase hydration of acetylene is determined not only by their ability to activate acetylene. The second probable condition for this process is the action of the catalyst on the reacting particles of water, which perhaps consists in further polarization of the adsorbed water under the influence of the ions in the lattice of the catalyst or carrier. This facilitates reaction of the water with the activated particles of acetylene.

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## DIENE HYDROCARBONS FROM UNSATURATED ALCOHOLS

### IV. CATALYTIC DEHYDRATION OF 2-METHYL-2-PENTEN-1-OL\*

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Leningrad State University

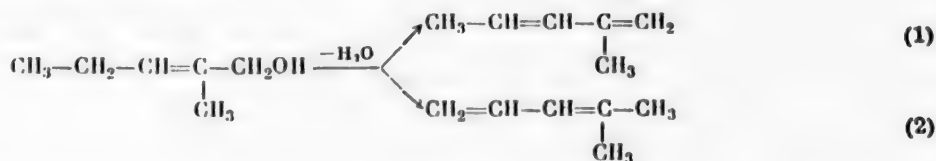
Translated from *Zhurnal Obshchei Khimii*, Vol. 30, No. 11, pp. 3826-3831,

November, 1960

Original article submitted October, 27, 1959

As was shown earlier [1, 2],  $\alpha, \beta$ -unsaturated alcohols under the action of dehydrating catalysts easily form diene hydrocarbons with conjugated systems of double bonds. One of such alcohols, 2-methyl-2-penten-1-ol, is not sufficiently described in the literature; data are given only for the boiling point of this alcohol, but these are contradictory [3-5]. There is no information in the literature as to its dehydration. Thus, it seems desirable to characterize 2-methyl-2-penten-1-ol in more detail and to investigate its dehydration.

On dehydration of 2-methyl-2-penten-1-ol we can expect formation of the conjugated dienes with the composition  $C_6H_{10}$ : 2-methyl-1,3-pentadiene (1) and 4-methyl-1,3-pentadiene (2).



As the dehydration catalysts we used the phosphate catalyst used in the synthetic rubber industry for preparing divinyl from 1,3-butyleneglycol (F) [17], and one of the dehydrating components of the S. V. Lebedev catalyst ( $B_2$ ) [1].

We have shown in the present work that in dehydration of 2-methyl-2-penten-1-ol there is formed a diene hydrocarbon  $C_6H_{10}$ , which is confirmed by determination of molecular weight and elementary composition. However, dehydration takes place differently on the catalysts used (see Table 1).

On the phosphate catalyst there is formed comparatively pure 2-methyl-1,3-pentadiene, whose presence was confirmed by the following results: a) boiling point, density, and index of refraction of the hydrocarbon which we obtained agreed with the literature data for 2-methyl-1,3-pentadiene; b) hydrogenation of the hydrocarbon over platinum black showed that it contained two double bonds, and isolation of the hydrogenation product, identified as 2-methylpentane, showed the structure of the hydrocarbon skeleton corresponding to that of the starting alcohol; c) formation of an adduct with maleic anhydride showed the presence of a conjugated system of double bonds, and by calculation on  $C_6H_{10}$  its content was 98.1%; from the melting point of the crystalline adduct it was the adduct of 2-methyl-1,3-pentadiene.

On catalyst  $B_2$  2-methyl-1,3-pentadiene was also formed, not alone, but with an admixture. The presence of 2-methyl-1,3-pentadiene in this case was confirmed by obtaining the corresponding adduct with maleic

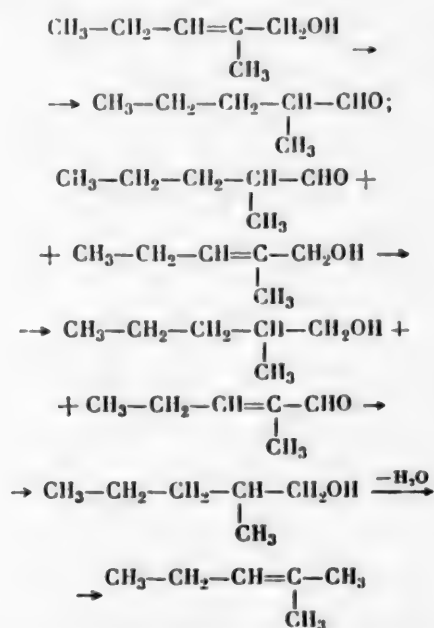
\* Presented at the All-Union Conference on Organic Catalysis in Moscow, November 18, 1959.

TABLE 1  
Characteristics of the Hydrocarbons Obtained

	B.p.	$d_4^{20}$	$n_D^{20}$	$MW$	$EMW$	% C	% H	% $C_6H_{10}$ (by hydro- genation)	M	M.p. of ad- duct with maleic anhydride
Hydrocarbon obtained on catalyst:										
F	73.5-75°	0.7150	1.4440	30.52	1.55	87.54	12.26	98.0	80.3	56.5°
$B_2$	73-74.5	0.6959	1.4200	30.01	1.04	86.75	12.24	70.9	79.8	56.2
Literature data for:										
2-methyl-1,3-pentadiene [6]	75.6-75.7	0.7196	1.4467	28.97		87.72	12.27		82.15	56-57 [8]
4-methyl-1,3-pentadiene [7]	76.4-76.9	0.7183	1.4525	(calc.)		(calc.)	(calc.)		(calc.)	Polymer [6, 9, 10]

anhydride which agreed in melting point with the adduct of 2-methyl-1,3-pentadiene, and the absence of depression of the melting point of a sample mixed with the adduct from the hydrocarbon obtained on the phosphate catalyst (sample melted at 56°). At the same time, the low values for boiling point, density, and index of refraction and also the low content of carbon (1%) showed the presence of an admixture in the diene hydrocarbon. There is no basis for assuming that this admixture is 4-methyl-1,3-pentadiene, isomer (2), since the data for the boiling point, density, and index of refraction of this hydrocarbon are close to or somewhat above those for 2-methyl-1,3-pentadiene (see Table 1).

The decrease in degree of unsaturation in the hydrogenation of this hydrocarbon (71%) shows the probable presence of an olefin hydrocarbon. The isolated hydrogenation product, 2-methylpentane, indicates that during the reaction there was no change in the carbon skeleton. Thus, in the experiment with catalyst  $B_2$  along with 2-methyl-1,3-pentadiene there is formed an olefin hydrocarbon  $C_6H_{12}$  with the same carbon skeleton. Since the position of the double bond in the hydrocarbon  $C_6H_{12}$  was not established experimentally, we can only make suggestions as to its structure. Of the possible structures for the hydrocarbon  $C_6H_{12}$ : 4-methyl-1-pentene, 4-methyl-2-pentene, 2-methyl-1-pentene, and 2-methyl-2-pentene, the formation of the latter is the most likely. Hydrocarbons with the double bond near the middle part of the molecule are more stable [11]. The appearance of 2-methyl-2-pentene could be explained by the following transformations of 2-methyl-2-penten-1-ol.



Thus, the chief product of the dehydration of 2-methyl-2-penten-1-ol over the catalysts studied is 2-methyl-1,3-pentadiene, a hydrocarbon which would naturally be expected\* by analogy with the catalytic dehydration of other  $\alpha,\beta$ -unsaturated alcohols under the same conditions [1, 2].

\* 4-Methyl-1,3-pentadiene if it were formed would be a hydrocarbon resulting from isomerization of 2-methyl-1,3-pentadiene, the original product of dehydration of the unsaturated alcohol.

The results of this work can be compared with the data obtained by Yu. A. Gorin and O. M. Nelmark previously [12] in the study of the transformation of primary propyl alcohol under the conditions of the S. V. Lebedev process. These authors found in the products of the transformation 2-methyl-1,3-pentadiene and 2-methylpentene. Later Yu. A. Gorin suggested a scheme [13] which explained these reactions. The formation of 2-methyl-1,3-pentadiene from *n*-propyl alcohol over the S. V. Lebedev catalyst was considered to occur through the intermediate formation of 2-methyl-2-penten-1-ol. The results obtained in the present work can serve as experimental confirmation of this idea.

The study of the catalytic dehydration of 2-methyl-2-penten-1-ol and the data from our previous investigations [1, 2] on dehydration of  $\alpha$ ,  $\beta$ -unsaturated alcohols from the point of view of the mechanism of splitting out water again confirm the unreality of the scheme of Ostromyslenskii [14], according to which dehydration should occur through a stage of an allene compound, which is structurally impossible in the case of an alcohol which has an alkyl group as the substituent on the  $\alpha$ -carbon atom.

## EXPERIMENTAL

2-Methyl-2-penten-1-ol was synthesized by selective reduction of the corresponding unsaturated aldehyde. 2-Methyl-2-penten-1-ol was obtained (415 g) by condensation of propionaldehyde by the action of 1 N NaOH [5]. B. p. 134-137°,  $d_4^{20}$  0.8588,  $n_D^{20}$  1.4476. According to the literature: b. p. 136.4-137.1°,  $d_4^{20}$  0.8581,  $n_D^{20}$  1.4488 [15].

2-Methyl-2-penten-1-al was reduced with lithium aluminum hydride in ether solution. The yield of impure unsaturated alcohol was 65-69 mole %.\* After drying over calcined potash, the product of the reduction was distilled on a column with effectiveness of 20 theoretical plates and the fraction 153.5-156° was isolated (most of it boiled at 154.5-155°); this was 2-methyl-2-penten-1-ol, whose yield was 48-52 mole % calculated on the unsaturated aldehyde taken.

B. p. 154.5-155°,  $d_4^{20}$  0.8536,  $n_D^{20}$  1.4425,  $M_R$  31.06; calc. 30.97.

Found %: C 71.81; H 12.10; OH 17.19.  $C_6H_{12}O$ . Calculated %: C 71.95; H 12.08; OH 16.98.

$\alpha$ -Naphthylurethane, long white needles, m. p. 93° (from ligroin).

Found %: N 5.50.  $C_{17}H_{18}O_2N$ . Calculated %: N 5.22.

According to the literature, b. p. 144-160° [3], 166-169° [4], 140-141° [5].

The unsaturation of the product was determined by the bromide-bromate method. We found 99.6%  $C_6H_{12}O$  in the substance studied.

A sample of 2-methyl-2-penten-1-ol (4 g) was exhaustively hydrogenated over platinum black and the hydrogenation product was isolated. It was 2-methyl-1-pentanol. B. p. 147°, 147°,  $d_4^{20}$  0.8269,  $n_D^{20}$  1.4176. According to the literature: b. p. 148°,  $d_4^{20}$  0.8263,  $n_D^{20}$  1.4182 [16].

Catalytic dehydration of 2-methyl-2-penten-1-ol was carried out in the apparatus described before [1]. The liquid formed a two-layer condensate. No gas formation was observed. The lower water layer of the condensate was separated and discarded, and the oily layer after drying with potash was analyzed for its content of hydroxyl groups [18] for quantitative determination of unreacted alcohol. Then the alcohol was removed as the borate ester [19] for which the oily layer was distilled over boric acid, which was taken in an amount somewhat greater than was required by the calculation for the formation of the triborate. The results of the experiment are given in Table 2.

We should note that the yield of hydrocarbon is given as calculated on the diene hydrocarbon  $C_6H_{10}$ . The yield of diene hydrocarbon on catalyst  $B_2$  was lower.

After separation of unreacted alcohol the hydrocarbon was dried with calcined potash and distilled over metallic sodium on a column with an effectiveness of 20 theoretical plates.

We distilled 11.36 g of hydrocarbon obtained on the phosphate catalyst into fractions (shown in weight %): 1st, to 73.5°, 5.8%,  $n_D^{20}$  1.4435; 2nd, 73.5-75°, 64.5% (constants given in Table 1); residue 10.6%,  $n_D^{20}$  1.4444; loss 19.1%.

\* Green and Hickinbottom found a yield of 86% [5].

We also fractionated 8.4 g of hydrocarbon obtained on catalyst B<sub>2</sub>: 1st, 70-72.5°, 16.6%,  $n_D^{20}$  1.4100; 2nd, 72.5-73.0, 14.3%,  $n_D^{20}$  1.4200; 3rd, 73.0-74.5°, 41.6% (constants given in Table 1); residue 8.2%,  $n_D^{20}$  1.4220, loss 19.3%.

Hydrogenation of the second fraction obtained on the phosphate catalyst, run over platinum black by the method of S. V. Lebedev [20], showed that the content of the hydrocarbon C<sub>8</sub>H<sub>10</sub> in the sample was 98.0%. The hydrogenation product was isolated (yield 88%), dried with calcium chloride, and distilled over metallic sodium; the main part of the substance came over at 62-62.5°. Then the hydrogenation product was characterized by basic constants and elementary analysis.

b. p. 62-62.5°,  $d_4^{20}$  0.6591,  $n_D^{20}$  1.3721.  $M_R$  29.70; calc. 29.91.

Found %: C 83.60; H 16.66. C<sub>8</sub>H<sub>14</sub>. Calculated %: C 83.62; H 16.37.

According to the literature for 2-methylpentane: b. p. 62.3-63.3°,  $d_4^{20}$  0.6599,  $n_D^{20}$  1.3735 [21].

Hydrogenation of the third fraction obtained on catalyst B<sub>2</sub> was carried out by analogy with the preceding. From the quantity of hydrogen absorbed the calculated content of hydrocarbon C<sub>8</sub>H<sub>10</sub> was 70.9%. The isolated hydrogenation product was identified as 2-methylpentane.

b. p. 62-62.5°,  $n_D^{20}$  1.3720.

Found %: C 83.49; H 16.30. C<sub>8</sub>H<sub>14</sub>. Calculated %: C 83.62; H 16.37.

Reaction with maleic anhydride was carried out under the conditions analogous to those described previously [6, 9]. The adduct was a crystalline derivative with a slight admixture of polymeric product in the case of catalyst B<sub>2</sub>. The adduct was washed free of maleic anhydride with hot water and recrystallized three times from ligroin.

In the fraction 73.5-75° obtained from the phosphate catalyst we determined the content of diene hydrocarbon by condensation with maleic anhydride [22] with later removal of unreacted hydrocarbon in a vacuum (1 mm) to constant weight of the adduct. The diene content with conjugated bonds was 98.1% (by weight).

TABLE 2

Catalytic Dehydration of 2-Methyl-2-penten-1-ol

Expt. No.	Catalyst	Temperature of experiment	Rate of adding alcohol (ml/hr/ml catalyst)	Alcohol passed (in g)	Unreacted alcohol (in %)	Hydrocarbon obtained (in g)	Yield of hydrocarbon calculated on C <sub>8</sub> H <sub>10</sub> (in mole %)	
							on decomposed alcohol	on alcohol passed
1	F	280°	0.34	42.68	10.1	29.9	94.9	85.4
2	B <sub>2</sub>	350	1.00	38.41	6.5	29.1	70.1	65.5

#### SUMMARY

1. We have carried out catalytic dehydration of 2-methyl-2-penten-1-ol over the phosphate catalyst used in the German synthetic rubber industry for preparing divinyl from 1,3-butyleneglycol and over one of the dehydrating components of the S. V. Lebedev catalyst (B<sub>2</sub>).

2. The chief product of dehydration of 2-methyl-2-penten-1-ol is 2-methyl-1,3-pentadiene. When dehydrating component B<sub>2</sub> is used there is an admixture of an olefin hydrocarbon C<sub>8</sub>H<sub>12</sub> which has the same carbon skeleton. The formation of the olefin hydrocarbon is explained by the transformations typical for the S. V. Lebedev catalyst.

3. Comparison of the results of our work with data on the transformation of n-propyl alcohol under conditions of the S. V. Lebedev process confirm the suggestion of Yu. A. Gorin that this transformation occurs through intermediate formation of 2-methyl-2-penten-1-ol.



4. The study of the catalytic dehydration of 2-methyl-2-penten-1-ol and the data from preceding investigations on the dehydration of  $\alpha, \beta$ -unsaturated alcohols confirm the unreality of the scheme of Ostromyslenskii, according to which dehydration should occur through a stage of an allene compound.

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## SYNTHESES IN THE PYRIMIDINE SERIES

### I. N-(2-PYRIMIDYL)-AMINO ACIDS

I. Kh. Fel'dman and Chih Chung-chi

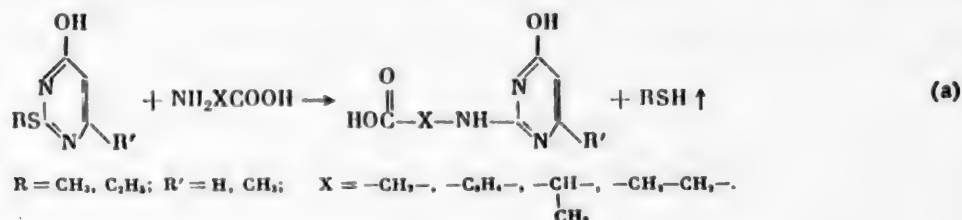
Leningrad Chemicopharmaceutical Institute

Translated from *Zhurnal Obshchei Khimii*, Vol. 30, No. 11, pp. 3832-3835,

November, 1960

Original article submitted December 22, 1959

For the study of the biological activity of pyrimidine derivatives we have prepared a series of N-(2-pyrimidyl)amino acids and their esters (Table 1 and 2). As starting substances for the work we used 2-alkylmercapto-6-hydroxypyrimidines which were obtained by the method described in the literature [1, 2]. The reaction of 2-alkylmercaptopyrimidines with amino acids (a) was carried out in water solution on a boiling water bath during several hours.



In carrying out the reaction in an acid or alkaline medium hydrolysis occurs and uracil or the corresponding 4-methyluracil are formed. In this study we used glycine,  $\alpha$ -aminopropionic acid,  $\beta$ -aminopropionic acid, and p-aminobenzoic acid. The investigation showed that under the conditions of our experiment glycine reacted best of all the aliphatic amino acids with the 2-alkylmercapto-6-hydroxypyrimidines used, and  $\alpha$ -aminopropionic acid the worst. p-Aminobenzoic acid also reacted well. Under the same reaction conditions, reaction of 2-alkylmercapto-6-hydroxypyrimidine with serine, leucine, or glutamic acid did not occur and uracil (or the corresponding 4-methyluracil) was formed as a hydrolysis product of the 2-alkylmercapto-6-hydroxypyrimidine used in the reaction.

In the hydrolysis of the resulting N-(6-hydroxy-2-pyrimidyl)-amino acids or N-(4-methyl-6-hydroxy-2-pyrimidyl)-amino acids with 5% sodium hydroxide, uracil (4-methyluracil) was formed. N-(4-Methyl-6-hydroxy-2-pyrimidyl)- $\alpha$ -aminopropionic acid even with long boiling in water was hydrolyzed with formation of 4-methyluracil. Under these conditions N-(4-methyl-6-hydroxy-2-pyrimidyl)-p-aminobenzoic acid did not hydrolyze.

The action of methyl (ethyl) alcohol on N-(6-hydroxy-2-pyrimidyl)-amino acids or N-(4-methyl-6-hydroxy-2-pyrimidyl)-amino acids in the presence of dry hydrogen chloride led to formation of the ester hydrochloride, which easily hydrolyzed in water solution. Such esterification could also occur with N-(4-methyl-6-hydroxy-2-pyrimidyl)-p-aminobenzoic acid. At the same time, experiments on the esterification with methyl or ethyl alcohols of N-(6-hydroxy-2-pyrimidyl)- $\alpha$ -aminopropionic acid and N-(4-methyl-6-hydroxy-2-pyrimidyl)- $\alpha$ -aminopropionic acid showed that here there was splitting out of the amino acid, forming uracil (4-methyluracil). However, in the ethyl (methyl) ester of N-(4-methyl-6-hydroxy-2-pyrimidyl)-p-aminobenzoic acid the

TABLE 1

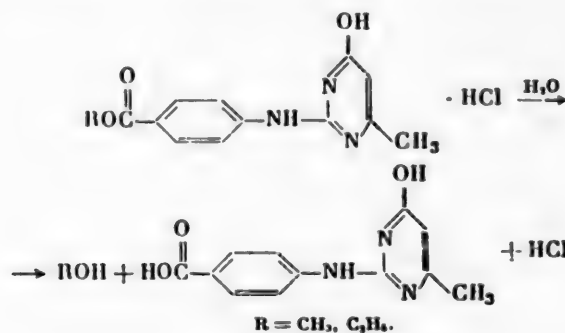
## N-(2-Pyrimidyl)-amino Acids

Substance No.	Substance obtained	M. p. (with decomposition)	Yield (in %)	%N	
				found	calculated
I	N-(6-Hydroxy-2-pyrimidyl)-aminoacetic acid*	270°	94.6	24.99 25.12 24.91	24.87
II	N-(4-Methyl-6-hydroxy-2-pyrimidyl)-aminoacetic acid**	268	79.8	23.22 23.12	22.96
III	N-(6-Hydroxy-2-pyrimidyl)- $\alpha$ -aminopropionic acid**	229-233	74.5	23.00 22.97	22.96
IV	N-(4-Methyl-6-hydroxy-2-pyrimidyl)- $\alpha$ -aminopropionic acid**	274-276	48.0	21.45 21.60	21.33
V	N-(6-Hydroxy-2-pyrimidyl)- $\beta$ -aminopropionic acid*	267-269	86.0	22.97 22.91	22.96
VI	N-(4-Methyl-6-hydroxy-2-pyrimidyl)- $\beta$ -aminopropionic acid**	249-250	80.0	21.85 21.78	21.33
VII	N-(4-Methyl-6-hydroxy-2-pyrimidyl)-p-aminobenzoic acid*	307-308	89.5	16.61	16.31

\* Insoluble in cold water, difficultly soluble in hot water. Purified by solution in 10% soda with later isolation with acetic acid.

\*\* Soluble in hot water and 50% alcohol, crystallized from alcohol.

amide bond is quite stable. When we heat the hydrochloride of the methyl (ethyl) ester of N-(4-methyl-6-hydroxy-2-pyrimidyl)-p-aminobenzoic acid with water on a boiling water bath for a half hour, there occurs hydrolysis of the ester group only (b)



(b)

## EXPERIMENTAL

N-(6-Hydroxy-2-pyrimidyl)-amino acids and N-(4-methyl-6-hydroxy-2-pyrimidyl)-amino acids (I-VII, Table 1). In a round-bottomed flask fitted with a reflux condenser were placed equimolecular amounts of 2-alkylmercapto-6-hydroxypyrimidine (or 2-alkylmercapto-4-methyl-6-hydroxypyrimidine), the amino acid (aminoacetic,  $\alpha$ -aminopropionic,  $\beta$ -aminopropionic, and p-aminobenzoic), and water (20 ml per 0.01 g mole). The mixture was heated on a boiling water bath for 40-60 hr. The alkyl mercaptan was then evolved. After cooling,

TABLE 2

Hydrochlorides of Esters of N-(2-Pyrimidyl)-amino Acids

Sub- stance No.	Substance obtained	M.p.	Yield (in %)	% N	
				found	calc.
VIII	Methyl N-(6-hydroxy-2-pyrimidyl)-aminoacetate hydrochloride	205-207°	66.7	19.04, 19.31	19.18
IX	Ethyl N-(6-hydroxy-2-pyrimidyl)-aminoacetate hydrochloride	207-208	62.5	18.31, 17.91	18.03
X	Methyl N-(4-methyl-6-hydroxy-2-pyrimidyl)-aminoacetate hydrochloride*	190-192	60.1	18.00, 17.80	18.03
XI	Ethyl N-(4-methyl-6-hydroxy-2-pyrimidyl)-aminoacetate hydrochloride	175-177	71.4	16.90, 16.76	17.00
XII	Ethyl N-(6-hydroxy-2-pyrimidyl)- $\beta$ -amino-propionate hydrochloride	163.5-164.5	23.2	16.96, 17.20	17.00
XIII	Ethyl N-(4-methyl-6-hydroxy-2-pyrimidyl)- $\beta$ -aminopropionate hydrochloride	179-180	22.8	16.01, 16.05	16.03
XIV	Methyl N-(4-methyl-6-hydroxy-2-pyrimidyl)-p-aminobenzoate hydrochloride	245-248	75.0	14.55, 14.03	14.21
XV	Ethyl N-(4-methyl-6-hydroxy-2-pyrimidyl)-p-aminobenzoate hydrochloride	241-243	81.4	13.58, 13.68	13.65

\* This ester was purified by solution in methyl alcohol and precipitation by ether.

the precipitate which formed was filtered off, washed with alcohol and ether, and crystallized from the corresponding solvent. All the N-(2-pyrimidyl)-amino acids were white substances insoluble in the usual organic solvents.

Methyl (ethyl) esters of N-(6-hydroxy-2-pyrimidyl)-amino acid and N-(4-methyl-6-hydroxy-2-pyrimidyl)-amino acid hydrochlorides. (VIII-XV, Table 2). In a round-bottomed three-neck flask fitted with a reflux condenser with a calcium chloride tube, and a stirrer was placed 0.01 g mole of N-(6-hydroxy-2-pyrimidyl)-amino acid [or N-(4-methyl-6-hydroxy-2-pyrimidyl)-amino acid] and 20 ml of anhydrous methyl (ethyl) alcohol. The reaction mixture was stirred on a boiling water bath and dry hydrogen chloride was passed through the mixture for 3-4 hr. After cooling, the precipitate [ester of N-(6-hydroxy-2-pyrimidyl)-amino acid] was separated. The resulting product recrystallized from methyl (ethyl) alcohol, appeared as white crystalline plates, soluble in water and alcohol, difficultly soluble in acetone, insoluble in benzene and ether.

Hydrolysis of N-(6-hydroxy-2-pyrimidyl)-amino acids and N-(4-methyl-6-hydroxy-2-pyrimidyl)-amino acids. In a round-bottomed flask fitted with a reflux condenser was placed 0.01 g mole of N-(6-hydroxy-2-pyrimidyl)-amino acid [or N-(4-methyl-6-hydroxy-2-pyrimidyl)-amino acid] and 20 ml of 5% sodium hydroxide solution. The mixture was heated for half an hour on a boiling water bath. After cooling, acetic acid was added to the solution to an acid reaction. The precipitate which came down was dried in a desiccator. The hydrolysis product had m. p. 330-335° (decomposition) (uracil) or the corresponding 270-280° (decomposition) (4-methyluracil). Analysis of the product for nitrogen and determination of the mixed melting point with uracil or 4-methyluracil confirmed that hydrolysis had occurred [4].

#### SUMMARY

1. We have worked out a new method for synthesis of N-(6-hydroxy-2-pyrimidyl)-amino acids, which consists in replacing alkylmercapto groups by amino acids by heating in water. However, with some amino acids 2-alkylmercapto-6-hydroxypyrimidine and 2-alkylmercapto-4-methyl-6-hydroxypyrimidine do not react under these conditions; the alkylmercapto group is hydrolyzed and in its place is formed a hydroxy group.

2. We have studied the properties of the hydrolysis product of N-(6-hydroxy-2-pyrimidyl)-amino acids and N-(4-methyl-6-hydroxy-2-pyrimidyl)-amino acids and their esters.

3. We have obtained fourteen new, undescribed compounds.

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# SYNTHESES IN THE PYRIMIDINE SERIES

## II. SUBSTITUTIONS IN POSITIONS 2 AND 6 OF PYRIMIDINE

N. Kh. Fel'dman and Chih Chung-chi

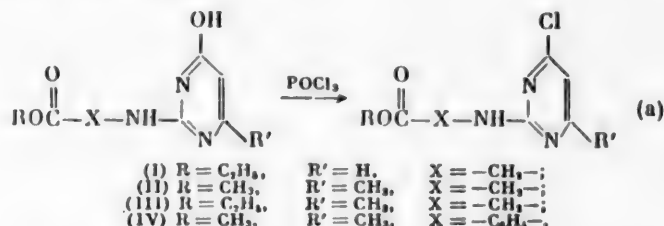
Leningrad Chemcopharmaceutical Institute

Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 11, pp. 3835-3839,

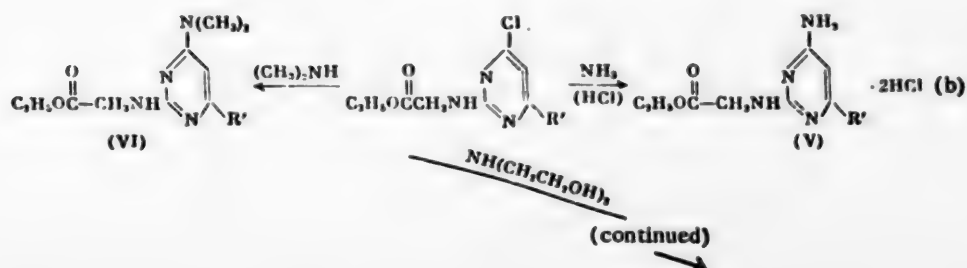
November, 1960

Original article submitted December 22, 1959

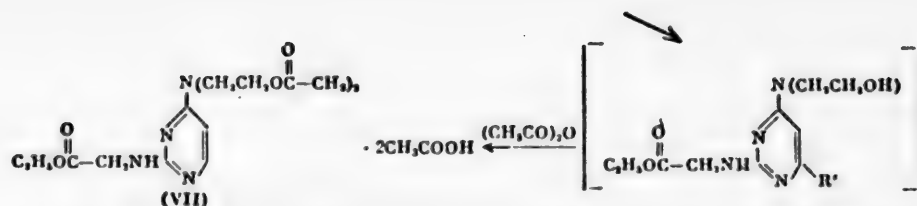
In the previous communication [1] we published the synthesis of N-(6-hydroxy-2-pyrimidyl)-amino acids and their esters, starting substances for preparing further pyrimidine derivatives which have amino acid ester radicals in position 2 and other substituents in position 6. The synthesis of the latter was carried out through esters of N-(6-chloro-2-pyrimidyl)-amino acids. The reaction of esters of N-(6-hydroxy-2-pyrimidyl)-amino acids with phosphorus oxychloride was carried out by heating on a boiling water bath with formation of esters of N-(6-chloro-2-pyrimidyl)-amino acids (a)



The earlier investigation [1] showed the instability of the amide bond in esters of N-(6-hydroxy-2-pyrimidyl)-amino acids. However, the stability of this bond is increased in esters of N-(6-chloro-2-pyrimidyl)-amino acids which are not decomposed by 0.1 N HCl in the cold. In the reaction of ammonia or dimethylamine with esters of N-(6-chloro-2-pyrimidyl)-aminoacetic acid (I) in anhydrous alcohol in a sealed tube, chlorine is replaced by ammonia or dimethylamine, forming the corresponding ester of N-(6-amino-2-pyrimidyl)-aminoacetic acid (V) and N-(6-dimethylamino-2-pyrimidyl)-aminoacetic acid (VI). A similar reaction of the same substances with diethanol amine led to formation of an especially hygroscopic noncharacterized product. Only acetylation of the latter permitted isolation of the corresponding acetate esters of N-(6-diacetoxydiethylamino-2-pyrimidyl)-aminoacetate acetate (VII) (VIII).

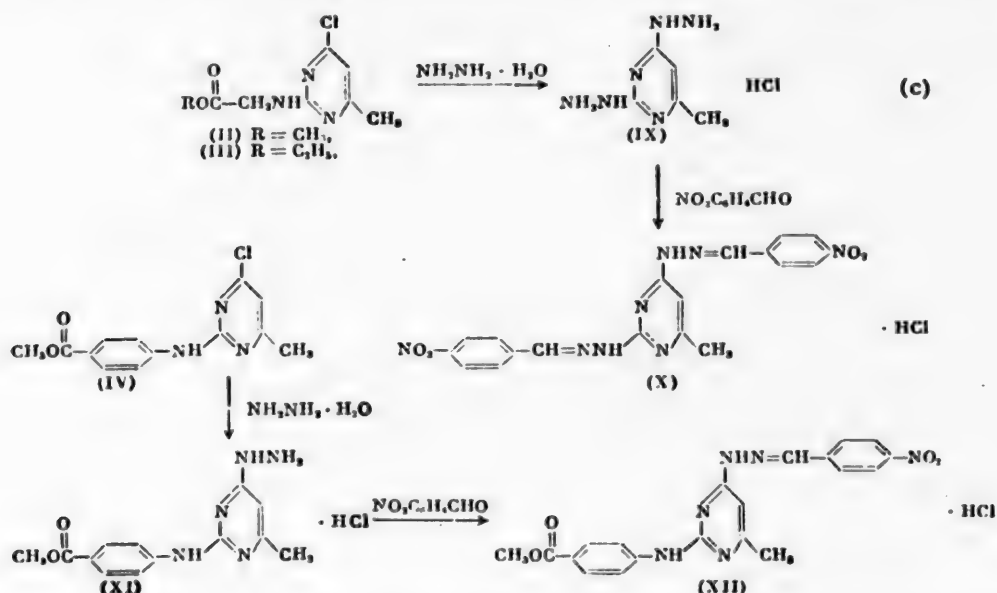






We observed that esters of N-(4-methyl-6-chloro-2-pyrimidyl)-aminoacetic acid (II) (III) react with hydrazine by boiling in alcohol to form 2,6-dihydrazido-4-methylpyrimidine hydrochlorides (IX). For confirmation of the structure of the latter it underwent reaction with p-nitrobenzaldehyde [2]. Elementary analysis of the product which was obtained confirmed the presence of the expected dibenzylidene compound (X). The reaction of methyl N-(4-methyl-6-chloro-2-pyrimidyl)-p-aminobenzoate (IV) with hydrazine even with heating in a sealed tube for 6 hr (120-130°) resulted only in the formation of methyl N-(4-methyl-6-hydrazido-2-pyrimidyl)-p-aminobenzoate hydrochloride (XI).

To show the structure of the resulting reaction products we also prepared their benzylidene derivatives (XII).



Hence it is evident that the amide bond in the esters of N-(6-chloro-4-methyl-2-pyrimidyl)-p-amino-benzoic acid (IV) and also the chlorine in position 6 are more stable than in esters of N-(6-chloro-2-pyrimidyl)-aminoacetic acid (II) (III).

#### EXPERIMENTAL\*

**Ethyl N-(6-chloro-2-pyrimidyl)-aminoacetate (I).** In a round-bottomed flask fitted with a reflux condenser with a calcium chloride tube was placed 0.03 g mole of ethyl N-(6-hydroxy-2-pyrimidyl)-aminoacetate hydrochloride and 0.10 g mole of phosphorus oxychloride. The reaction mixture was heated on a water bath for five hr. The excess phosphorus oxychloride was distilled off in a vacuum and the residue was poured onto ice; the resulting solution was made alkaline with ammonia and extracted three times with ether, 20 ml each time. The combined ether extracts were dried with anhydrous sodium sulfate; after distillation of the ether we obtained a residue which was crystallized from alcohol. The white plates which separated were well soluble in ether, benzene, and hot alcohol, and insoluble in water. Yield 61%, m. p. 75.5-76.5°.

By this method we also obtained methyl and ethyl esters of N-(4-methyl-6-chloro-2-pyrimidyl)-aminoacetic acid (II and III). Yield of (II) 39.6%, m. p. 102-104°. Yield of (III) 40.0%; m. p. 74.5-75.5°.

\* Results of analyses given in table.

Sub- stance No.	Formula	% N	
		found	calculated
(I)	$C_8H_{10}O_2N_3Cl \cdot$	19.90, 20.12	19.48
(II)	$C_8H_{10}O_2N_3Cl$	19.33, 19.00	19.49
(III)	$C_8H_{12}O_2N_3Cl$	18.57, 18.40	18.23
(IV)	$C_{13}H_{12}O_2N_3Cl$	15.14, 15.28	15.15
(V)	$C_8H_{12}O_2N_4 \cdot 2HCl$	20.53, 20.45	20.23
(VI)	$C_{10}H_{16}O_2N_4$	24.98, 25.10	24.98
(VII)	$C_{16}H_{14}O_6N_4 \cdot 2CH_3COOH$	11.47, 11.53	11.47
(VIII)	$C_{17}H_{16}O_6N_4 \cdot 2CH_3COOH$	10.93, 10.86	11.05
(IX)	$C_5H_{10}N_6 \cdot HCl$	44.38, 44.69	44.21
(X)	$C_{19}H_{16}O_4N_8 \cdot HCl$	24.35, 24.60	24.34
(XI)	$C_{13}H_{15}O_2N_5 \cdot HCl$	22.61, 22.41	22.62
(XII)	$C_{20}H_{17}O_4N_8 \cdot HCl$	18.70, 18.99	19.00

\* Found %: Cl 16.96, 17.30. Calculated %: Cl 16.60.

Methyl N-(4-methyl-6-chloro-2-pyrimidyl)-p-aminobenzoate (IV). In a round-bottomed flask fitted with a condenser with a calcium chloride tube was placed 3.0 g of methyl N-(4-methyl-6-hydroxy-2-pyrimidyl)-p-aminobenzoate hydrochloride and 10.1 g of phosphorus oxychloride. The reaction mixture was heated on a boiling water bath for six hr and after cooling was poured onto ice; the resulting solution was made alkaline with ammonia at 10-15°. The resulting precipitate was filtered off and crystallized from benzene. We obtained a white crystalline powder which melted at 218-220° (decomposition). Insoluble in water and alcohol, soluble in hot benzene and ether. Yield 2.0 g (72.2%).

Ethyl N-(6-amino-2-pyrimidyl)-aminoacetate hydrochloride (V). A sealed tube in which were placed 0.9 g of ethyl N-(6-chloro-2-pyrimidyl)-aminoacetate and 7 ml of anhydrous alcohol saturated with ammonia was heated in a tube furnace at 125-130° for three hr. After cooling, the reaction mixture from the tube was distilled to 1/3 its volume and then 6 ml of absolute ether saturated with hydrogen chloride was added. The precipitate which came down was twice recrystallized from alcohol. The resulting white crystals, m. p. 114-116°, were soluble in water, hot alcohol, and acetone, insoluble in ether and benzene. Yield 1.1 g (87.4%).

Ethyl N-(6-dimethylamino-2-pyrimidyl)-aminoacetate (VI). A sealed tube in which were placed 0.9 g of dimethylamine dissolved in 5 ml of anhydrous alcohol and 0.87 g of ethyl N-(6-chloro-2-pyrimidyl)-aminoacetate was heated for three hr at 125-130°. After cooling the contents of the tube were treated with 1.0 g of soda and the mixture was well shaken and filtered; the filtrate was evaporated to a thick consistency and mixed with 4 ml of ether saturated with hydrogen chloride. The precipitate was filtered off and dissolved in alcohol which was made alkaline with ammonia; the white crystalline powder was filtered off; m. p. 190-192°, soluble in ether and hot alcohol, insoluble in water. Yield 0.8 g (92.4%).

Ethyl N-(6-diacetoxydiethylamino-2-pyrimidyl)-aminoacetate acetate (VII). A sealed tube in which were placed 0.02 g mole of ethyl N-(6-chloro-2-pyrimidyl)-aminoacetate (I), 0.02 g mole of diethanolamine, 0.5 g of triethylamine, and 2.0 ml of anhydrous alcohol was heated at 135-145° for three hr. After cooling, the contents of the tube were poured into a flask and well shaken with 1.5 g of anhydrous soda. After removal of the precipitate the filtrate was freed from triethylamine by distillation. The resulting thick residue was treated with 15 ml of acetic anhydride, after which the mixture was heated at 50-55° for three hr. The excess acetic anhydride was removed in a vacuum, the precipitate was twice recrystallized from dry acetone. The product was obtained as white needles with m. p. 253-255°. It was well soluble in water, alcohol, and hot acetone, insoluble in ether and benzene. Yield 55.5%.

By this method we also obtained the acetate of ethyl N-(4-methyl-6-diacetoxydiethylamino-2-pyrimidyl)-aminoacetate (VIII). Yield 50.0%, m. p. 249-251°.

2,6-Dihydrazido-4-methylpyrimidine hydrochloride (IX).\* In a round-bottomed flask fitted with reflux condenser we placed 0.43 g of methyl (or 0.47 g of ethyl) N-(4-methyl-6-chloro-2-pyrimidyl)-aminoacetate (II or III), 5 ml of alcohol, and 0.2 g of hydrazine hydrate; the mixture was heated on a boiling water bath for 2.5 hr. After cooling, white crystals came down and were filtered off and crystallized from alcohol. The product was well soluble in water and hot alcohol, insoluble in ether and benzene. Yield 0.68 g (76.0%), m. p. 199-200°.

\* The base of this product was obtained from 2,6-dichloro-4-methylpyrimidine with m. p. 213° [3].

2,6-DI-(p-nitrobenzaldehydehydrazono)-4-methylpyrimidine hydrochloride (X). In a round-bottomed flask we dissolved 0.1 g of 2,6-dihydrazido-4-methylpyrimidine hydrochloride (IX) in 5 ml of hot alcohol. To the solution we added 0.15 g of p-nitrobenzaldehyde in 2 ml of alcohol. The mixture stood for a day, and the orange precipitate was filtered and washed with ether. The product was obtained as red-orange crystals with m. p. 240-242° (decomposition). It did not dissolve in ordinary organic solvents or cold water.

Methyl N-(4-methyl-6-hydrazido-2-pyrimidyl)-p-aminobenzoate hydrochloride (XI). We placed in a sealed tube 1.4 g of methyl N-(4-methyl-6-chloro-2-pyrimidyl)-p-aminobenzoate (X), 0.5 g of hydrazine hydrate, and 25 ml of absolute alcohol. The tube was heated at 120-130° for six hr. All the product dissolved. After cooling, the precipitate which came down was filtered and crystallized from a 10% alcoholic solution of hydrogen chloride. The resulting white product with m. p. 245-247° (decomposition) was easily soluble in water, more difficultly so in alcohol and benzene, and insoluble in ether. Yield 1.2 g (82.0%). We obtained its p-nitrobenzaldehydehydrazone (XII). This was a yellow powder with m. p. 278-279° soluble in hot alcohol, more difficultly soluble in cold water and alcohol, insoluble in ether and benzene.

#### SUMMARY

1. We have showed that replacement of the hydroxyl group in esters of N-(6-hydroxy-2-pyrimidyl)-aminoacetic acid by chlorine raises the stability of the amide bond to hydrolysis.
2. We have established that the replacement of chlorine by amines in esters of N-(4-methyl-6-chloro-2-pyrimidyl)-p-aminobenzoic acid occurs with more difficulty than in esters of N-(4-methyl-6-chloro-2-pyrimidyl)-aminoacetic acid. In the first case more severe conditions are required than in the second.
3. The amide bond in esters of N-(4-methyl-6-chloro-2-pyrimidyl)-aminoacetic acid is unstable and when hydrazine hydrate acts on it, 2,6-dihydrazido-4-methylpyrimidine is obtained.
4. Starting from esters of N-(6-hydroxy-2-pyrimidyl)-amino acids we have prepared eleven undescribed esters of N-(2-pyrimidyl)-amino acids which are substituted in position 6 by different groups.

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## CARBON SUBOXIDE AND SOME OF ITS REACTIONS

### VIII. THE REACTION OF CARBON SUBOXIDE WITH ALICYCLIC AND AROMATIC AMINES AND A SERIES OF THEIR SUBSTITUENTS

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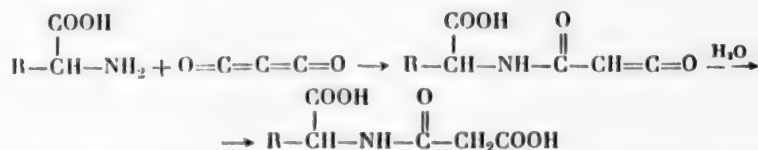
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November, 1960

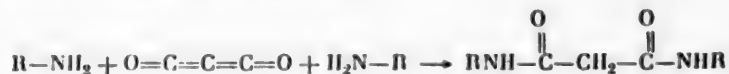
Original article submitted December, 14, 1959

The reaction of carbon suboxide with alicyclic amines and aniline, as is known, leads to formation of the corresponding malonyl diamide. The amine reacts with carbon suboxide in the cold instantaneously with practically quantitative yields. However, as the literature data indicate [1, 2],  $\alpha$ -amino acids of the aliphatic series can react with only one ketone group of carbon suboxide, as a result of which there is first formed a substituted aminocarbonylcarbamethylene which is hydrolyzed to malonyl monoamide. The investigations mentioned were carried out on a series of  $\alpha$ -amino acids. Here the reaction took place according to the following scheme:



Evidently this particular addition of the malonyl group using carbon suboxide is due to the influence of the electrophilic carboxyl group which strongly decreases the reactivity of the primary amine group.

In this connection there is considerable interest in the degree of influence of different electrophilic substituents in alicyclic and aromatic amines on the reactivity of carbon suboxide. In the present study it has been shown experimentally that the simplest alicyclic amines and esters of aminocyclohexane carboxylic acid at ordinary temperature in absolute ether quickly form with carbon suboxide the corresponding malonyl-bis-substituted amides. There is also almost no effect on the great reactivity of carbon suboxide by the naphthalene ring and even by the presence of alkoxy groups in aniline. Under much more severe conditions reaction of carbon suboxide with isomers of alkylaminobenzoates and aminoacetophenone occurs. This is also true of sulfanilic with blocked sulfo groups (sulfanilamide). However, in the latter case only the malonyl-bis-substituted amide is formed. Reaction occurs according to the scheme:



The reaction of carbon suboxide with isomers of aminobenzoic acid, with sulfanilic acid, and with isomers of nitroaniline could not be carried out to give either malonyl monoamide or the malonyl-bis-substituted amides.

Starting from the nature of the chemical structure, we must assume that some of the compounds synthesized will have definite pharmacological properties.

## EXPERIMENTAL

The reaction of carbon suboxide with amines was carried out in absolute diethyl ether in the cold or at the temperature of boiling ether. If the reaction took place with heating we added 10-20 mg of p-toluenesulfonic acid to the reaction mixture as a catalyst. In all the experiments we used gaseous carbon suboxide obtained either by pyrolysis of diacetylvinyl anhydride [3] or by pyrolysis of diethyloxalyl acetate [3, 4].

The starting amines were obtained by the methods described in the literature: cyclopentylamine with b. p. 106-108° from cyclopentanone oxime [5]; cyclohexylamine with b. p. 133-134° from cyclohexanone oxime [5]; *l*-methylamine with b. p. 205-206° from *l*-menthone ketoxime [6]; *d, l*-bornylamine with m. p. 162-163° from *d, l*-camphoroxime [6]; methyl ester of *o*-aminocyclohexanecarboxylic acid with b. p. 114-117° (17-18 mm) from methyl anthranilate [7]; methyl ester of *p*-aminocyclohexane carboxylic acid from methyl *p*-aminobenzoate [7]; methyl *o*-aminobenzoate with m. p. 22-24° from anthranilic acid [8]; ethyl *p*-aminobenzoate with m. p. 90-91° from *p*-aminobenzoic acid [8]; *o*-aminoacetophenone with m. p. 18-19° from *o*-nitroacetophenone [9]; *m*-aminoacetophenone with m. p. 99° from *m*-nitroacetophenone [9]; *p*-aminoacetophenone with m. p. 105-106° from *p*-nitroacetophenone [9]; and we also used carefully purified commercial preparations of  $\alpha$ -naphthylamine,  $\beta$ -naphthylamine, *o*-anisidine, *p*-anisidine, *p*-phenetidine, *p*-aminobenzenesulfonamide; isomers of aminobenzoic acid and nitroaniline.

N,N'-Malonyl-bis-cyclopentylamine (I). We added 1.4 g of cyclopentylamine to a solution of 0.71 g of carbon suboxide in 100 ml of ether. A white crystalline precipitate at once came down and on the next day was separated and recrystallized twice from alcohol, washed with ether, and dried. A further amount of the substance was isolated from the ether mother liquors. The substance was soluble in hot acetone and alcohol, insoluble in water. In an analogous way we obtained N,N'-malonyl-bis-cyclohexylamine (II).

N,N'-Malonyl-bis-*l*-menthylamine (III). We added 1.7 g of *l*-menthylamine to a solution of 0.75 g of carbon suboxide in 100 ml of ether. The mixture stood for a day, but no precipitate appeared. Then the ether was distilled off completely and the residue, a sticky, transparent mass, was heated for one hour with water. The water was separated and the solidified product was twice recrystallized. It was soluble in alcohol, less so in ether, insoluble in water.

In the same way we obtained N,N'-malonyl-bis-*d, l*-bornylamine (IV).

N,N'-Malonyl-bis-methyl ester of *o*-aminocyclohexane carboxylic acid (V). We added 0.8 g of the methyl ester of *o*-aminocyclohexane carboxylic acid to a solution of 0.3 g of carbon suboxide in 35 ml of ether. The precipitate was separated after two hours and washed with ether. The substance was insoluble in water and poorly soluble in alcohol.

N,N'-Malonyl-bis-methyl ester of *p*-aminocyclohexane carboxylic acid (VI) was obtained like the preceding.

N,N'-Malonyl-bis- $\alpha$ -aminonaphthalene (VII). To 1.0 g of  $\alpha$ -naphthylamine was added 50 ml of an ether solution of 0.3 g of carbon suboxide. After short shaking, a precipitate appeared which stood for 1 hr and was then filtered off. The evaporated ether mother liquor gave a further quantity of the substance. The compound was poorly soluble in alcohol and ether, insoluble in water. N,N'-Malonyl-bis- $\beta$ -aminonaphthalene (VIII) was obtained in the same way.

N,N'-Malonyl-bis-*o*-anisidine (IX). We added 1.0 g of *o*-anisidine to a solution of 0.3 g of carbon suboxide in 40 ml of ether. The mixture was shaken for several minutes and after three hr the precipitate was separated. The evaporated ether mother liquor could give a further amount of the substance. The product was soluble in warm alcohol and acetone, less so in ether, insoluble in water. In an analogous way we obtained N,N'-malonyl-bis-*p*-anisidine (X) and N,N'-malonyl-bis-*p*-phenetidine (XI).

N,N'-Malonyl-bis-methyl *o*-aminobenzoate (XII). Through a solution of 1.8 g of methyl *o*-aminobenzoate in 80 ml of ether was passed evenly and slowly for 16 hr a stream of carbon suboxide (1.9 g of C<sub>3</sub>O<sub>2</sub>). The mixture was heated on a water bath heated to 80-90°. After passage of carbon suboxide was stopped, heating was continued for two hours more. Then the ether was evaporated and the yellow solid residue was heated for 1 hr with water; the water was separated and the substance was recrystallized three times from methanol. The product was soluble in acetone and alcohol, partly soluble in ether, insoluble in water. In an analogous way we obtained N,N'-malonyl-bis ethyl-*p*-aminobenzoate (XIII).



Sub- stance No.	Yield, %	M.p.	Solvent for crystallization	Empirical formula	Results of analysis, %						Molecular weight	
					C		H		N		found	calc.
					found	calc.	found	calc.	found	calc.	found	calc.
I	87	164-169°	Ethanol	$C_{10}H_{12}N_2O_2$	66.01	65.6	9.31	9.2	11.44	11.8	154	156
II	91	173-174	The same	$C_{15}H_{18}N_2O_2$	68.9	67.4	5.56	5.33	7.78	8.3	225	228
III	72.5	150-151	"	$C_{21}H_{24}N_2O_2$	73.2	73.0	10.9	11.1	7.3	7.3	378	378
IV	52	130-132	"	$C_{23}H_{26}N_2O_2$	73.8	73.9	10.35	10.2	7.7	7.5	379	374
V	95	144-144.5	Ether	$C_{16}H_{20}N_2O_6$	60.0	59.7	7.4	7.65	7.4	7.35	379	382
VI	90	194-200	The same	$C_{19}H_{20}N_2O_6$	59.5	59.7	7.8	7.65	7.5	7.35	374	382
VII	91	226-227	"	$C_{23}H_{18}N_2O_2$	78.1	77.9	5.5	5.1	7.5	7.8	350	354
VIII	87	231-232.5	"	$C_{23}H_{18}N_2O_2$	78.3	77.9	5.3	5.1	7.8	7.8	357	354
IX	66.5	159-160	Ethanol	$C_{17}H_{18}N_2O_4$	65.2	64.9	6.1	5.7	9.2	8.9	317	314
X	72	223-224	Methanol	$C_{17}H_{18}N_2O_4$	65.3	64.9	5.8	5.7	9.1	8.9	318	314
XI	71.5	225-226	The same	$C_{19}H_{22}N_2O_4$	66.9	66.6	6.3	6.4	8.1	8.2	339	342
XII	24	152-153	"	$C_{19}H_{22}N_2O_6$	62.0	61.6	4.8	4.9	7.7	7.6	366	370
XIII	57.5	205-206	"	$C_{21}H_{22}N_2O_6$	62.6	62.8	5.7	5.5	7.1	7.0	401	398
XIV	38	160-161	"	$C_{19}H_{18}N_2O_4$	67.3	67.4	5.5	5.3	8.5	8.3	341	338
XV	48	173-174	"	$C_{19}H_{18}N_2O_4$	67.6	67.4	5.5	5.3	8.7	8.3	339	338
XVI	50	211-212	"	$C_{19}H_{18}N_2O_4$	67.8	67.4	5.7	5.3	7.9	8.3	343	338
XVII	42.5	271-272	Ethyl acetate	$C_{15}H_{10}O_6N_4S_2$	—	—	—	—	11.2	11.4 (S 15.2)	418	412 (S 15.5)

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**N,N'-Malonyl-bis-o-aminoacetophenone (XIV).** Through 1.5 g of o-aminoacetophenone in 40 ml of ether for 7-8 hr we passed a stream of carbon suboxide (2.1 g of  $C_3O_2$ ). Further treatment was as above. The resulting substance was soluble in dioxane, acetone, and hot alcohol, less so in ether, insoluble in water. In the same way we obtained N,N'-malonyl-bis-aminoacetophenone (XV) and N,N'-malonyl-bis-p-aminoacetophenone (XVI). As described above we obtained N,N'-malonyl-bis-p-aminobenzenesulfonamide (XVII). The product was soluble in acetone, and alcohol, less so in ether, soluble in hot water.

The yields, melting points, solvents for crystallization and results of analyses of the above substances are given in the table.

When a stream of carbon suboxide was passed for 15-20 hr with heating through ether solutions of o-, m-, and p-aminobenzoic acids, o- and p-nitroaniline, and sulfanilic acid, the reaction mixtures became somewhat cloudy and formed a small amount of polymeric carbon suboxide. We could not isolate any malonyl substituted amides.

#### SUMMARY

1. We have obtained several undescribed N,N'-malonyl-bis-substituted amides by the action of ether solutions of carbon suboxide on a series of alicyclic and aromatic amines and also their derivatives.

2. In some cases it was shown that the presence of alkyl and even of ester groups in the ring of the alicyclic amines had little effect on the reactivity of carbon suboxide. In substituted anilines, ester and acetyl groups somewhat lowered this reactivity.

3. Carboxyl, nitro and sulfo-substituted anilines in ether solution did not react with carbon suboxide.

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## LETTERS TO THE EDITOR

### ENERGY OF REPULSION IN IONIC MOLECULES

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The bond energy in molecules of gaseous alkali halides can be calculated on the basis of ionic models [1-3].

The expression for the energy of repulsion in this case can be in the form  $Ae^{-r/\rho}$  where  $A$  and  $\rho$  are constants determined by Rittner for experimental data ( $r_e$  and  $k_e$ ) [1]. Until recently,  $\rho$  was considered the same for all molecules. We have shown that  $\rho$  depends on the type of ions of the molecule, increasing from  $Li^+$  to  $Cs^+$  and from  $F^-$  to  $I^-$  [3, 4]. The same is found for thallium halides (I) [5].

Since the possibility was shown for calculating the energy on the basis of an ionic model for halides of the II A group [6], it is of interest to calculate  $\rho$  depending on this type of ion.

The expression  $Ae^{-r/\rho}$  or  $Ae^{-br}$  (where  $b = 1/\rho$ ) reflects the exponential character of change in wave function with distance [7]. The change found in  $\rho$  (or  $b$ ) in the series  $F^- \rightarrow I^-$  or  $Li^+ \rightarrow Cs^+$  can be expressed as follows.

According to Slater the wave function of the ion  $\psi_i = s^{n^*-1} e^{-\frac{Z_{ef} r}{n^* a_0}} = s^{n^*-1} e^{-b_i r}$ , where

$$b_i = \frac{Z_{ef} r}{n^* a_0}, \quad (1)$$

and  $s$  is the distance of the electron from the nucleus [8].

The energy of repulsion of cation and anion equals  $P e^{-(b_k + b_A) \cdot r}$ , where  $P$  is the polynomial from  $r$  which changes very little compared to the exponential factor and the corresponding constant  $A$  [9].

Hence we can assume that in  $Ae^{-br}$  the value

$$e^{-br} = e^{-(b_k + b_A)r} \text{ and } b = b_k + b_A. \quad (2)$$

It follows from (1) that there is a regular change in  $b$  in the series of ions, and from (2) that there is a regular change in  $\rho$ . For calculation of  $b_i$  as a standard we take the molecule of KCl ( $b = 2.915$ ), consisting of isoelectronic ions. For such ions from (1) it follows

$$\frac{b_i}{b_j} = \frac{Z_{ef} r_i}{Z_{ef} r_j}. \quad (3)$$

In the case of KCl,  $b_{K^+} = 1.673$ ,  $b_{Cl^-} = 1.242$ .

We find the individual  $b_i$  for the other ions of alkali metals and halogens from (2), using  $b$  for nine molecules calculated by us from experimental data. Thus  $b_i$  and  $\rho$  are calculated for the remaining molecules (see table).

Coefficient  $\rho \cdot 10^{11}$  (experimental values given in italics)

	$F^- \quad b_i = 1.392$	$Cl^- \quad b_i = 1.242$	$Br^- \quad b_i = 1.071$	$I^- \quad b_i = 0.834$
$Li^+ \quad b_i = 1.855$	308	323	<i>345</i>	<i>379</i>
$Na^+ \quad b_i = 1.770$	316	<i>332</i>	<i>346</i>	<i>384</i>
$K^+ \quad b_i = 1.673$	326	<i>343</i>	<i>374</i>	<i>399</i>
$Rb^+ \quad b_i = 1.575$	<i>357</i>	<i>355</i>	<i>379</i>	<i>415</i>
$Cs^+ \quad b_i = 1.528$	<i>342</i>	<i>361</i>	<i>385</i>	<i>423</i>
$Fr^+ \quad b_i = 1.50$	<i>346</i>	<i>365</i>	<i>389</i>	<i>428</i>
$Be^{2+} \quad b_i = 2.542$	254	264	<i>277</i>	<i>296</i>
$Mg^{2+} \quad b_i = 2.029$	292	<i>306</i>	<i>323</i>	<i>338</i>
$Ca^{2+} \quad b_i = 1.889$	<i>305</i>	<i>319</i>	<i>337</i>	<i>367</i>
$Sr^{2+} \quad b_i = 1.746$	<i>319</i>	<i>335</i>	<i>355</i>	<i>387</i>
$Ba^{2+} \quad b_i = 1.693$	<i>324</i>	<i>341</i>	<i>362</i>	<i>396</i>

The  $b_i$  of the ions of the alkaline earth metals is calculated by (3) through the  $b_i$  of the ions  $Li^+$ ,  $Na^+$ ,  $K^+$ ,  $Rb^+$ , and  $Cs^+$ . On this basis by (2) are calculated  $b$  and  $\rho$  of molecules of group II A halides (see table).

Calculation of the bond energy on the basis of the value obtained for  $\rho$  gives good results. The average variation of the calculated value for the bond energy from the experimental is 2% for 20 molecules of alkali metals and 2.5% for 9 molecules of group II A halides for which the experimental values are known.

We use an analogous method for some other molecules, for example,  $ZnCl_2$ .

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## THE MECHANISM OF ADDITION OF LITHIUM ALKYL TO ENYNE HYDROCARBONS

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Lithium alkyls add to enyne hydrocarbons with formation, after treatment of the reaction mixture with water, of aliene hydrocarbons [1]. In order to explain the mechanism of this reaction we have studied the infrared spectra of solutions of lithium butyl and vinylacetylene in undecane and mixtures of undecane and ether (1:1).

In the first solvent the reaction occurs with low rate and after standing of the reaction mixture for a day (20") we still find in the spectrum the deformation frequency of vinylacetylene ( $906\text{ cm}^{-1}$ ). In the presence of ether the reaction takes place with heating and ends after several minutes.

After the reagents are mixed there slowly appears in the infrared spectrum, along with the frequencies of lithium butyl ( $857, 934, 965, 1026, 1048\text{ cm}^{-1}$ ) [2, 3] and of vinylacetylene ( $906, 967, 1605, 2226\text{ cm}^{-1}$ ), an intense band with a frequency  $1865\text{ cm}^{-1}$ , which grows stronger during the course of the reaction and which evidently corresponds to the associated molecule  $\text{C}_2\text{H}_5\text{-CLi=C=CH-CH}_2\text{-C}_4\text{H}_9$  (I). After 12 hr standing of the mixture the spectrum still shows one high frequency of  $1780\text{ cm}^{-1}$ . When the reaction mixture is treated with water at all stages of the reaction, this frequency disappears and we see the more or less intense frequency of the allene group  $1956\text{ cm}^{-1}$  and also the deformation frequency  $865\text{ cm}^{-1}$  [5] (intensity depending on depth of the reaction).

The ascription of the frequency  $1865\text{ cm}^{-1}$  to oscillation of the lithium-allene complex (I) is confirmed by the fact that this frequency of  $1865\text{ cm}^{-1}$  and also the frequency  $1780\text{ cm}^{-1}$  (on standing) appear in the spectrum of mixtures of a solution of lithium butyl and ethylbutylallene in undecane (when the reagents are mixed, heating occurs). When this solution is treated with water, ethylbutylallene is regenerated, and by treatment with  $\text{CO}_2$  an allenic acid is obtained which shows the process of metallation [probably forming a compound of type (I)].

On the other hand, enyne hydrocarbons which do not form allenes in the reaction with lithium alkyls (for example, allyl-tert-butylacetylene) give complexes which absorb not at  $1865\text{ cm}^{-1}$ , but evidently at  $2050\text{ cm}^{-1}$ .

These results confirm that the addition of lithium alkyls to vinylalkylacetylenes goes through a stage of formation of a lithium-allene compound. The allene group occurs in the process of addition of the lithium alkyl to the conjugated system and not when the reaction mixture is treated with water.

Diene hydrocarbons (isoprene, piperylene) also form complexes in the reaction with lithium butyl which are characterized by frequencies in the infrared spectra of about  $1780\text{ cm}^{-1}$ .

The intense frequency of the lithium complex can be used for study of the kinetics of the addition of lithium alkyls to unsaturated compounds.

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## ALYLATION OF TOLUENE BY PROPYLENE ON AN ALUMINOSILICATE CATALYST

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We have established the possibility of alkylation of toluene by propylene in the presence of industrial granular aluminosilicate catalyst in a streaming gas phase at atmospheric pressure in order to obtain cymene in high yield. As is known, cymene can be used as a starting source for the production of phthalic acid by oxidizing it with oxygen of the air.

The alkylation of toluene by propylene is carried out in an apparatus of the flowing type [1] on an aluminosilicate catalyst with the composition (%): 14.01  $\text{Al}_2\text{O}_3$ , 84.66  $\text{SiO}_2$ , 0.36  $\text{Na}_2\text{O}$ , 0.13  $\text{Fe}_2\text{O}_3$ , 0.60  $\text{CaO}$ , Zn, trace, MgO, trace. The toluene used is chemically pure: b. p.  $111^\circ$ ,  $d_4^{20}$  0.868,  $n_D^{20}$  1.4970. Propylene is obtained by dehydration of isopropyl alcohol over aluminum oxide at  $380^\circ$ .

We have found that at  $300^\circ$ , mole ratio of toluene to propylene 3:1, and volume rate of supplying toluene to the reactor of 0.45 volumes per volume of catalyst in one hour, the yield of cymene based on propylene used in the reaction is 77%, and the yield of trialkylbenzenes is 2.5%.

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## DISCUSSION

### THE HEAT OF FORMATION OF NIOBIUM PENTOXIDE

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 11, pp. 3847-3848,  
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In a recently published paper of Morozova and Getskina [1] results were given on the investigation of the heats of formation of niobium oxides. The authors established in particular that the heat of formation of  $\text{Nb}_2\text{O}_5$  from the elements was 472.5 kcal/g-mole. This value was obtained on the basis of data on the heat of combustion of preparations containing 98.5% Nb (with a calculated correction for impurities). At about the same time we carried out a study of the heats of formation of oxides and carbides of niobium [2]. In this we also used a metal containing 98.52% Nb. The treatment of the results of calorimetric investigation led us to a value for the heat of formation of  $\text{Nb}_2\text{O}_5$  of 458.6 kcal/g-mole.

The considerable difference in the results of [1] and [2] forced us to make new measurements using a purer metal (99.01% Nb, 0.94% Ta, 0.04% O; Ti, Fe, Si, and C not detected) ignited near the melting point.

We carried out two sets of experiments with later controls for the complete oxidation of niobium. We showed that in the first set of experiments this was 99.33% and in the second, 99.10%.

In treatment of the experimental data we introduced corrections for incomplete oxidation of the metal and for the presence of tantalum and oxygen in the starting material. Here it was assumed that the tantalum was completely burned to  $\text{Ta}_2\text{O}_5$  with a heat effect of 499 kcal/g-mole [3] and the oxygen formed a solid solution in niobium whose heat of formation (per g-atom O) was close to the heat of formation of NbO from the elements [4] (which we studied earlier [2]).

A summary of the original calorimetric data and also of the corrections in them are given in the table.

The data of the table show that the heat of formation of niobium pentoxide is  $\Delta H \approx -455.1 \pm 0.5$  kcal/g-mole which is not a bad agreement with our previous results [2] and with the data of Humphrey [5].

Set of experiments	Heat of combustion (in cal/g of starting preparation)	Correction (in cal/g of starting preparation)		Heat of combustion in cal/g Nb	Heat of formation of $\text{Nb}_2\text{O}_5$ (in kcal/g-mole)
		unoxidized	for Ta and O		
I	2419.86	16.32	16.06	2452.24	455.7
II	2408.50	21.87	15.99	2446.36	454.6
					455.1 $\pm$ 0.5

The absence in publication [1] of an indication of the original results of the calorimetric measurements and the method of calculation of the heat of oxidation of the carbon contained in the metal does not permit us to establish the reason for the difference remarked above. In this connection it is very desirable to have



additional control measurements since the values used for  $\Delta H$  of  $Nb_2O_5$  are basic for the determination of the heat of formation of the lower oxides of niobium, and also for the carbides, nitrides, and other compounds.

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## THE REASON FOR THE HEAT OF FORMATION OF NIOBIUM PENTOXIDE

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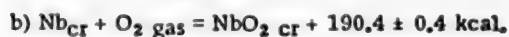
Previously for the heat of formation of  $Nb_2O_5$  the following values have been presented:  $463.2 \pm 4$  kcal/g-formula (Becker and Roth [1]) and 455.2 kcal/g-formula (Humpherey [2]). M. P. Morozova and L. L. Getskina [3] found for the heat of combustion of powdered niobium to  $Nb_2O_5$   $472.6 \pm 1.0$  kcal/g-formula. In the same work the heat of burning  $NbO_2$  was found to be  $37.0 \pm 0.4$  kcal/g-formula, which agreed very well with the value of  $36.67 \pm 0.10$  kcal/g-mole found by A. D. Mah [4].

This fact and the fact that determination of the heat of combustion of titanium [5] and its oxides carried out in the same apparatus used for determination of the heat of combustion of niobium [3] agreed with the values found by Humpherey [6] led us to assume that the difference in data for  $Nb_2O_5$  obtained by M. P. Morozova and L. L. Getskina [3] and the data of F. G. Kusenko and P. V. Gel'd [7] and Humpherey [2] was not related to the different method of calorimetric determination.

Actually, repetition of the calorimetric experiments with powdered niobium used in work [3] led to a value for heat of combustion which was obtained by M. P. Morozova and L. L. Getskina [3], namely  $473.2 \pm 0.8$  kcal/g-formula.

On the other hand, compact niobium which contained 0.01% C, 0.5% Ta (with corrections for the presence of these impurities and for incomplete combustion) gave for the heat of formation of  $Nb_2O_5$  a value of  $454.8 \pm 0.8$  kcal/g-formula, which agrees well with the data of work [2] and [7].

If we accept the value for the heat of formation for  $NbO_{2.5}$  of  $227.4 \pm 0.4$  kcal, then we must correct the heat of formation of  $NbO$  and  $NbO_2$ . They are:



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## MORE ON THE QUESTION OF ADDITIVITY OF DENSITY

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Density is one of the comparatively few properties of solutions for which it is possible to determine entirely rigidly from this single property an expression which is based in the ideal case on additive properties. In the binary system formed without change in volume the dependence of density on composition is linear only when the latter is expressed in volume parts:

$$d = d_1 w_1 + d_2 w_2 \quad (1)$$

Although this expression (in a somewhat different form) was used by D. I. Mendeleev even in 1865 [1], many present day authors, as we have recently shown [2], still make the groundless assumption of the additivity of density in other methods of expressing composition, which sometimes leads to serious errors.

The correct conclusions from Eq. (1) are drawn in the recently published monograph of V. Ya. Anosov [3] on pages 13-14. However, before this conclusion (on page 12) and after it (on page 26) it is stated that the specific gravity (density) is additive if we express the concentration directly in mole parts. This statement is evidently an opinion of the author and is based on a pure misconception, since V. Ya. Anosov earlier often speaks of the need to use volume parts in this case [4, 5]. Properly speaking, the very formulation of the question of determining the rational method of expressing the composition in constructing a composition-properties diagram should be for V. Ya. Anosov to give.

The tradition of the investigation of specific gravity of solutions goes back to D. I. Mendeleev in Russia. The question of the additivity of densities of solutions is in essence relatively simple, and its correct solution should be accepted by all workers in this field.

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# Soviet Journals Available in Cover-to-Cover Translation

ABBREVIATION	RUSSIAN TITLE	TITLE OF TRANSLATION	PUBLISHER	TRANSLATION BEGAN
				Vol. Issue Year
AE	Atomnaya Energiya	Soviet Journal of Atomic Energy	Consultants Bureau	1 1 1956
Akust. zh.	Akusticheskie zhurnali	Soviet Physics - Acoustics	American Institute of Physics	1 1 1955
Astr.(on). zh(tum).	Antibiotiki	Antibiotics	Consultants Bureau	4 1 1959
Avto(mat). sverka	Astronomicheskie zhurnali	Soviet Astronomy-AJ	American Institute of Physics	34 1 1957
	Avtomaticheskaya svarka	Automatic Welding	British Welding Research Association (London)	
	Avtomatika i Telemekhanika	Automation and Remote Control	Instrument Society of America	1 1959
	Biofizika	Biophysics	National Institutes of Health*	27 1 1956
	Biokhimiya	Biochemistry	Consultants Bureau	21 1 1957
	Byulleten' eksperimental'noi biologii i meditsiny	Bulletin of Experimental Biology and Medicine	Consultants Bureau	41 1 1959
DAN (SSSR)				
Doklady AN SSSR	Doklady Akademii Nauk SSSR	The translation of this journal is published in sections, as follows:	American Institute of Biological Sciences	106 1 1958
		Doklady Biochemistry Section	American Institute of Biological Sciences	112 1 1957
		Doklady Biological Sciences Sections (includes: Anatomy, biophysics, cytology, ecology, embryology, endocrinology, evolutionary morphology, genetics, histology, hydrobiology, microbiology, morphology, parasitology, physiology, zoology sections)		
		Doklady Botanical Sciences Sections (includes: Botany, phytopathology, plant anatomy, plant ecology, plant embryology, plant physiology, plant morphology sections)	American Institute of Biological Sciences	112 1 1957
		Proceedings of the Academy of Sciences of the USSR, Section: Chemical Technology	Consultants Bureau	106 1 1956
		Proceedings of the Academy of Sciences of the USSR, Section: Chemistry	Consultants Bureau	106 1 1956
		Proceedings of the Academy of Sciences of the USSR, Section: Physical Chemistry	Consultants Bureau	112 1 1957
		Doklady Earth Sciences Sections (includes: Geochemistry, geology, geophysics, hydrogeology, mineralogy, paleontology, petrography, permafrost sections)		
		Proceedings of the Academy of Sciences of the USSR, Section: Geochemistry	American Geological Institute	124 1 1959
		Proceedings of the Academy of Sciences of the USSR, Section: Geology	Consultants Bureau	106- 1 1957- 123 6 1958
		Proceedings of the Academy of Sciences of the USSR, Sections: Geology	Consultants Bureau	106- 1 1957- 123 6 1958
		Doklady Soviet Mathematics	The American Mathematics Society	131 1 1961
		Soviet Physics-Doklady (includes: Aerodynamics, astronomy, crystallography, cybernetics and control theory, electrical engineering, energetics, fluid mechanics, heat engineering, hydraulics, mathematical physics, mechanics, physics, technical physics, theory of elasticity sections)		
		Proceedings of the Academy of Sciences of the USSR, Applied Physics Sections (does not include mathematical physics or physics sections)	American Institute of Physics	106 1 1956
		Wood Processing Industry	Consultants Bureau	106- 1 1956- 117 1957
		Telecommunications	Timber Development Association (London)	9 1959
		Entomological Review	Massachusetts Institute of Technology*	1 1957
		Pharmacology and Toxicology	American Institute of Biological Sciences	38 1 1959
		Physics of Metals and Metallurgy	Consultants Bureau	20 1 1957
		Sechenov Physiological Journal USSR	Acta Metallurgica*	5 1 1957
		Plant Physiology	National Institutes of Health*	1 1957
		Geochemistry	American Institute of Biological Sciences	4 1 1957
		Soviet Physics-Solid State	The Geochemical Society	1 1958
		Measurement Techniques	American Institute of Physics	1 1959
		Bulletin of the Academy of Sciences of the USSR: Division of Chemical Sciences	Instrument Society of America	1 1959
			Consultants Bureau	1 1952
Derevoobrabat. prom.-st.				
	Derevoobrabatkovayushchaya promyshlennost'			
	Elektritsiyaz			
	Entomologicheskoe obozrenie			
	Farmakologiya i toksikologiya			
	Fizika metallov i metallovedenie			
	Fiziologicheskii zhurnal im. I. M. Sechenova			
	Fiziologiya rastenii			
	Geokhimiya			
	Fizika tverdogo tela			
	Izmeritel'naya tekhnika			
	Izvestiya Akademii Nauk SSSR: Otdel. Khim. i Nukl.			

*continued*

Izv. AN SSSR, Otd. Tekhn. N(auk) Met(ali). I top.	(see Met. I top.)	Bulletin of the Academy of Sciences of the USSR: Physical Series	1	1954
Izv. AN SSSR Ser. fiz(ich).	Izvestiya Akademii Nauk SSSR: fizicheskaya	Bulletin (Festival) of the Academy of Sciences USSR: Geophysics Series	1	1954
Izv. AN SSSR Ser. geofiz.	Izvestiya Akademii Nauk SSSR: Seriya geofizicheskaya	Izvestiya of the Academy of Sciences of the USSR: Geologic Series	1	1958
Izv. AN SSSR Ser. geol.	Izvestiya geologicheskaya	Soviet Rubber Technology	18	1959
Kauch. I rez.	Kautchuk i rezina	Kinetics and Catalysis	1	1959
	Kinetika i kataliz	Coke and Chemistry USSR	3	1960
	Koks i khimiya	Colloid Journal	14	1958
Kolloidn. zh(urn).	Kolloidnyi zhurnal	Soviet Physics - Crystallography	2	1957
Metall. I term. obrabot. metal.	Kristallografiya	Metal Science and Heat Treatment of Metals	6	1958
Met. I top.	Metallurgiya i termicheskaya obrabotka metallov	Metallurgist	1	1957
Mikrobiol. OS	Metallurg	Russian Metallurgy and Fuels	1	1960
	Metallurgiya i topliva	Microbiology	26	1957
	Mikrobiologiya	Optics and Spectroscopy	6	1959
	Optika i spektroskopiya	Soviet Soil Science	1	1958
	Pochvovedenie	Instrument Construction	1	1958
	Priborostroenie	Instruments and Experimental Techniques	1	1957
Pribory i tekhn. eksperimenta)	Pribory i tekhnika eksperimenta	Applied Mathematics and Mechanics	1	1958
Prikl. matem. i mekh.	Prikladnaya matematika i mekhanika	Problems of the North	12	1957
PTÉ	(see Pribory i tekhn. éka.)	Radio Engineering	2	1957
Radiotekh.	Problemy Severa	Radio Engineering and Electronics	1	1959
Radiotekh. i élektronika	Radiotekhnika	Machines and Tooling	1	1959
	Stanki i instrument	Stal (In English)	1	1959
Slek. i keram.	Stal	Glass and Ceramics	13	1956
Svaroch. proizvo	Sleklo i keramika	Welding Production	4	1959
Teor. veroyat. i prim.	Svarochnoe proizvodstvo	Theory of Probability and Its Applications	1	1956
	Teoriya veroyatnosti i ee primeneniye	Nonferrous Metals	1	1960
Tsvet. Metall	Tsvetnye metally	Soviet Physics - Uspekhi (partial translation)	66	1958
UFN	Uspekhi fizicheskikh Nauk	Russian Chemical Reviews	15	1960
UKh	Uspekhi khimii	Russian Mathematical Surveys		
UMN	Uspekhi matematicheskikh nauk	Russian Review of Biology		
Usp. fiz. nauk	(see UFN)	Russian Engineering Journal		
Usp. khim(ii)	(see UKh)	Problems of Hematology and Blood Transfusion		
Usp. matem. nauk	(see UMN)	Problems of Oncology		
Usp. sovr. biol.	Usp. khim(ii)	Problems of Virology		
Vest. mashinostroeniya	Usp. fiz. nauk	Industrial Laboratory		
Vop. gem. i per. krovi	Usp. matem. nauk	Journal of Analytical Chemistry USSR		
	Vest. mashinostroeniya	Soviet Physics-JETP		
Vop. onk.	Voprosy gematologii i perelivaniya krovi	Russian Journal of Physical Chemistry		
Vop. virusol.	Voprosy onkologii	Journal of Microbiology, Epidemiology and Immunobiology		
Zavlodsk. lab(oratoriya)	Voprosy virusologii	The Russian Journal of Inorganic Chemistry		
Zh(urn) Zh. anal(it). khimii	Zavodskaya laboratoriya	Journal of General Chemistry USSR		
ZhETF	Zhurnal analiticheskoi khimii	Journal of Applied Chemistry USSR		
Zh. eksperim. i teor. fiz.	Zhurnal éksperimental'noi i teoreticheskoi fiziki	Journal of Structural Chemistry		
ZhFKh Zh. fiz. khimii	Zhurnal fizicheskoi khimii	Soviet Physics-Technical Physics		
ZhMEI Zh(urn). mikrobiol. épidemiol. i immunobiol.	Zhurnal mikrobiologii, épidemiologii i immunobiologii	Pavlov Journal of Higher Nervous Activity		
ZhNKh	Zhurnal neorganicheskoi khimii			
Zh(urn). neorgan(ich). khim(ii)				
ZhOKh	Zhurnal obshchei khimii			
ZhPKh	Zhurnal prikladnoi khimii			
Zh(urn). prikl. khimii				
ZhSKh	Zhurnal strukturnoi khimii			
Zh(urn). strukt. khimii				
ZhTF	Zhurnal tekhnicheskoi fiziki			
Zh(urn). tekhn. fiz.				
Zh(urn). vyssh. nervn. deyat. (im. Pavlova)	Zhurnal vysshei nervnoi deyatel'nosti (im. I. P. Pavlova)			

# SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY ENCOUNTERED IN SOVIET PERIODICALS

FIAN	Phys. Inst. Acad. Sci. USSR.
GDI	Water Power Inst.
GITI	State Sci.-Tech. Press
GITTL	State Tech. and Theor. Lit. Press
GONTI	State United Sci.-Tech. Press
Gosenergizdat	State Power Press
Goskhimizdat	State Chem. Press
GOST	All-Union State Standard
GTTI	State Tech. and Theor. Lit. Press
IL	Foreign Lit. Press
ISN (Izd. Sov. Nauk)	Soviet Science Press
Izd. AN SSSR	Acad. Sci. USSR Press
Izd. MGU	Moscow State Univ. Press
LEIIZhT	Leningrad Power Inst. of Railroad Engineering
LET	Leningrad Elec. Engr. School
LETI	Leningrad Electrotechnical Inst.
LEIIZhT	Leningrad Electrical Engineering Research Inst. of Railroad Engr.
Mashgiz	State Sci.-Tech. Press for Machine Construction Lit.
MEP	Ministry of Electrical Industry
MES	Ministry of Electrical Power Plants
MESEP	Ministry of Electrical Power Plants and the Electrical Industry
MGU	Moscow State Univ.
MKhTI	Moscow Inst. Chem. Tech.
MOPI	Moscow Regional Pedagogical Inst.
MSP	Ministry of Industrial Construction
NII ZVUKSZAPIOI	Scientific Research Inst. of Sound Recording
NIKI	Sci. Inst. of Modern Motion Picture Photography
ONTI	United Sci.-Tech. Press
OTI	Division of Technical Information
OTN	Div. Tech. Sci.
Stroizdat	Construction Press
TOE	Association of Power Engineers
TsKTI	Central Research Inst. for Boilers and Turbines
TsNIEL	Central Scientific Research Elec. Engr. Lab.
TsNIEL-MES	Central Scientific Research Elec. Engr. Lab.-Ministry of Electric Power Plants
TsVTI	Central Office of Economic Information
UF	Ural Branch
VIESKh	All-Union Inst. of Rural Elec. Power Stations
VNIIM	All-Union Scientific Research Inst. of Metrology
VNIIZhDT	All-Union Scientific Research Inst. of Railroad Engineering
VTI	All-Union Thermotech. Inst.
VZEI	All-Union Power Correspondence Inst.

Note: Abbreviations not on this list and not explained in the translation have been transliterated, no further information about their significance being available to us. - Publisher.





